APR 5 1952
HOSPITAL LIBRARY

Vol. 31 APRIL, 1952 No. 4

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

UNIVERSITY OF MICHIGAN HOSPITAL LIBRARY

EDITORS

ALTON OCHSNER, New Orleans OWEN H. WANGENSTEEN, Minneapolis

ASSOCIATE EDITORS

UNIVERSITY OF MICHIGAN LOCK, Baltimore I. S. RAVDIN, Philadelphia

JOHN R. PAINE, Buffalo

APR 15 1952

HOSPITAL LIBRARY

Original Communications

Aortography in Upper Gastrointestinal Hemorrhage. James A. Dolphin, M.D., Minneapolis, Minn., and Brian Williams, M.D., M.R.C.P., London, England -- 487

Treatment of Experimental Acute Pancreatitis With Banthine. William W. Shingleton, M.D., William G. Anlyan, M.D., and A. K. David, Jr., B.S., Durham, N. C. ---------- 490

Serum Amylase Levels in Experimental Pancreatitis. James R. Thistlethwaite, M.D., and Robert P. Hill, M.D., Washington, D. C. ---------- 495

Renogastroepiploic Anastomosis in the Treatment of Portal Hypertension. Raymundo de Britto, Octavio Vaz, Pedro Abdalla, and Rodrigues da Silva, Rio de Janeiro, Brazil ---------- 502

An Experimental Study of Protein and Fat Assimilation After Total Gastrectomy. Tilden C. Everson, M.D., Ph.D., Chicago, Ill. ---------- 511

The Effects of Partial Gastrectomy on Canine External Pancreatic Secretion. David Annis, M.B., F.R.C.S., and George A. Hallenbeck, M.D., Rochester, Minn. 517

Suppurative Pelvic Thrombophlebitis. IV. Results. Conrad G. Collins, M.D., Robert O. Norton, M.D., Edward W. Nelson, M.D., B. Bernard Weinstein, M.D., Jason H. Collins, M.D., and Herman D. Webster, Jr., B.S., New Orleans, La. ---------- 528

(Contents continued on inside back cover)

Published by THE C. V. MOSBY COMPANY, St. Louis, U. S. A.

Copyright 1952 by The C. V. Mosby Company

SURGERY

EDITORIAL BOARD

JOHN ADRIANI, New Orleans
EDWARD D. CHURCHILL, Boston
FREDERICK A. COLLER, Ann Arbor
MICHAEL DE BAKEY, Houston
CLARENCE E. DENNIS, Brooklyn
LESTER R. DRAGSTEDT, Chicago
ROBERT E. GROSS, Boston
EMILE F. HOLMAN, San Francisco
J. ALBERT KEY, St. Louis
EDWIN P. LEHMAN, University, Va.
JOHN J. MORTON, Rochester, N. Y.
CARL MOYER, St. Louis
THOMAS G. ORR, Kansas City, Kan.
GEORGE T. PACK, New York
WILDER G. PENFIELD, Montreal
WILLIAM F. RIENHOFF, JR., Baltimore

COMMITTEE ON PUBLICATIONS

ARTHUR W. ALLEN
Boston, Mass.

J. GARROTT ALLEN
Chicago, Ill.

WILLIAM A. ALTEMEIER
Cincinnati, Ohio

ISAAC A. BIGGER
Richmond, Va.

J. BARRETT BROWN
St. Louis, Mo.

ALEXANDER BRUNSCHWIG
New York, N. Y.

O. T. CLAGETT
Rochester, Minn.

WARREN H. COLE
Chicago, Ill.

C. D. CREEVY
Minneapolis, Minn.

DANIEL C. ELKIN
Atlanta, Ga.

FRANK GERBODE
San Francisco, Calif.

FRANK C. MANN
Rochester, Minn.

CHARLES W. MAYO
Rochester, Minn.

H. THOMAS RANDALL
New York, N. Y.

LEO G. RIGLER
Minneapolis, Minn.

MAURICE B. VISSCHER
Minneapolis, Minn.

A. EARL WALKER
Baltimore, Md.

JAMES C. WHITE
Boston, Mass.

PHILIP D. WILSON
New York, N. Y.

Vol. 31, No. 4, April, 1952. Surgery is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription price: United States, its possessions, Pan-American Countries, $12.00 a year; Canada and foreign, $13.00. Entered as Second-Class Matter January 20, 1937, at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Printed in the U. S. A.

SURGERY

VOL. 31 APRIL, 1952 No. 4

Original Communications

AORTOGRAPHY IN UPPER GASTROINTESTINAL HEMORRHAGE

AN EXPERIMENTAL STUDY

JAMES A. DOLPHIN, M.D.,* MINNEAPOLIS, MINN., AND
BRIAN WILLIAMS, M.D., M.R.C.P.,** LONDON, ENGLAND

(From the Department of Surgery, University of Minnesota Medical School)

AORTOGRAPHY as a diagnostic aid was introduced first by dos Santos[1] in 1929. Its use in the field of urologic diagnosis has recently come to the fore through the efforts of Farinas,[2] Doss,[4] and Wagner.[5] For the abdominal surgeon its application has been limited to the demonstration of vascular abnormalities.

It is the purpose of this paper to report our brief experience with the method as applied to gastrointestinal tract hemorrhage in the dog. All appreciate the clinical value of a method which would differentiate arterial from venous bleeding. The demonstration by barium swallow of esophageal varices or of mucosal ulceration is a step in this direction. It was our feeling that if a radiopaque substance could be introduced into the arterial tree at the time of active bleeding, it might be possible to demonstrate the site of the arterial bleeding. Aortography seemed our logical avenue.

TECHNIQUE

Five mongrel dogs were anesthetized, using intravenous Nembutal. The right femoral artery was exposed and cannulized with a Polythene tubing, the end of which extended into the thoracic aorta. In three of the dogs, the right gastroepiploic artery was transected. The distal end was ligated and a rubber-shod bulldog clamp was applied to the proximal end. A gastrotomy incision was then made in the anterior wall of the stomach near the greater curvature and the severed proximal end of the artery was inserted into the gastric lumen. The vessel was secured in position by interrupted 00000 silk sutures between the perivascular fat and the stomach wall.

Received for publication, July 30, 1951.
*Department of Surgery, University of Minnesota.
**St. George's Hospital.

In the remaining two dogs, a major branch of the splenic artery, in addition to the right gastroepiploic artery, was transplanted into the gastric lumen using a similar technique. A gastric tube was positioned and 150 c.c. of air was injected into the stomach to provide a contrast medium in each of the five dogs. In the latter two, a ligature was placed loosely around the end of the splenic artery within the gastric lumen and secured to the gastric tube.

The animals were placed in the standard anteroposterior position. Preliminary flat films of the abdomen were made. In the first group of dogs, bleeding was obtained by releasing the rubber-shod clamp from the gastroepiploic artery. In the remaining two dogs the sudden removal of the gastric tube produced intragastric hemorrhage from the transplanted splenic artery.

Immediately upon removal of the clamp or the gastric tube 20 c.c. of 75 per cent Neo-Iopax* solution was injected into the aorta via the tubing through the femoral artery. Exposure was made during the injection of the dye, thus obtaining a standard, retrograde aortogram. Films were then obtained 15 to 20 seconds after completion of the injection. A third set of exposures were made at 3 and 7 minutes after injection.

Technical features depended upon the size and thickness of the dog, and as experience was gained, the following gave satisfactory detail and contrast in the film:

Time: 0.1 second
kv: 68-76
Ma: 50
Focal spot: 4.2 mm.
Fixed anode

All five dogs were sacrificed at the conclusion of the procedure. Ligatures were placed around the esophagogastric junction and the pylorus. The stomach was then removed and x-ray films made of its content.

OBSERVATIONS AND INTERPRETATION

Adequate delineation of the following vessels resulted: (a) thoracic and abdominal aorta, (b) splenic artery, (c) intercostal vessels, (d) the vascular circle of the stomach (The left and right gastric arteries were well outlined. Visualization was less complete in the region of the pylorus and duodenum than in the upper half of the stomach. The inflation with 150 c.c. of air led to improved detail but it remained difficult to identify the origin and course of the great number of fine vessels present in this region.), (e) the hepatic artery, (f) the superior mesenteric artery, (g) the inferior mesenteric artery, (h) the renal arteries, (i) aortic bifurcation with the iliac vessels.

In addition, concentration of the medium was sufficiently dense in the spleen and kidneys to give a precise idea of the size and integrity of contour of these viscera. The spleen, which occupies a central position at the level of the lower half of the stomach, was less clearly defined than the kidneys. It was observed that the anteroposterior position was not the one of choice for

*Supplied for this study by Schering Corporation, Bloomfield, N. J.

complete delineation of the renal vessels or for adequate profile nephrograms. Better results are given with the tube angled some 15 to 20° transversely and 10° toward the head. In man, the anteroposterior view remains the most satisfactory for revealing the course of the renal vessels and for nephrograms.

The duodenum in the dog appears to be directed posteriorly and the line of demarcation between the pylorus and the first part of the duodenum is indistinct from the radiologic viewpoint. These considerations make it unlikely that small amounts of pooled contrast medium will ever be demonstrated by this method.

The pool of contrast medium will, by gravitation, appear at the lower pole of the stomach. Immediate dilution of the drug will be an inevitable sequel but the danger of misinterpretation and the false assumption that such pools are composed of contrast medium was, in practice, the greater difficulty. It was impossible to conclusively demonstrate radiographically the presence of the dye in the stomach of any of the dogs. No information was gained by obtaining films of the clot removed from the excised stomach.

DISCUSSION

It is impossible from such brief experience to come to definite conclusions on the usefulness of aortography in gastrointestinal hemorrhage. It is our hope that the method used here may serve as a stimulus to broaden the applicability of aortography. Its use in intra- and retroperitoneal hemorrhage warrants investigation. Refinements of technique, and improvement in contrast medium might some day make feasible clinical application of aortography in a broad spectrum of disease.

REFERENCES

1. dos Santos, R., Lomas, A. C., and Coldas, J. P.: Arteriographie des Membres et de l'aorte Abdominal, Paris, 1931, Masson et Cie.
2. Farinas, P. L.: Retrograde Arteriography in the Study of the Abdominal Aorta and Iliac Arteries, SURGERY **18**: 244, 1945.
3. Farinas, P. L.: Retrograde Abdominal Aortography, Am. J. Roentgenol. **55**: 448, 1946.
4. Doss, A. K.: Translumbar Aortography; Diagnostic Value in Urology, J. Urol. **55**: 594, 1946.
5. Wagner, F. B.: Arteriography in Renal Diagnosis: Preliminary Report and Critical Evaluation, J. Urol. **56**: 625, 1946.

TREATMENT OF EXPERIMENTAL ACUTE PANCREATITIS WITH BANTHINE

WILLIAM W. SHINGLETON, M.D., WILLIAM G. ANLYAN, M.D., AND A. K. DAVID, JR., B.S., DURHAM, N. C.

(From the Department of Surgery, Duke University School of Medicine)

IT IS generally agreed that acute pancreatitis in man consists of two main clinical types. One, usually referred to as acute edematous pancreatitis, is a self-limited, relatively nonfatal disease that is commonly associated with acute or chronic cholecystic disease. It may become recurrent and lead to far-advanced disease of the pancreatic acini with consequent calcification of the organ, pancreatogenous diarrhea, diabetes, and intractable abdominal pain. A second clinical variety, usually referred to as acute hemorrhagic necrosis of the pancreas, is a severe, acute, highly fatal disease accompanied by shock and prostration and also leads to far-advanced damage to the pancreas if the patient survives.

Acute pancreatitis has been produced in the experimental animal in various ways and to varying degrees. One method of producing the disease is by ligation of the pancreatic duct in an animal whose pancreas is in an active phase of secretion, as recently reported by Lium and Maddock.[1] Pancreatitis produced in this manner resembles acute edematous pancreatitis of man. A much more severe disease somewhat resembling acute hemorrhagic necrosis of man can be produced experimentally in animals by ligation of the pancreatic duct and the retrograde injection of certain substances, such as bile and trypsin, into the duct, as first described by Opie.[2]

The common factor present in these two varieties of experimental pancreatitis is obstruction of the pancreatic duct. Theoretically, the human disease can be caused by obstruction of either the main pancreatic duct or the ampulla of Vater, the latter producing a regurgitation of bile into the pancreatic duct system and thus inducing the disease. Another important consideration in regard to both etiology and treatment is the role played by activated pancreatic enzymes in the presence of duct obstruction or regurgitation of bile. Continued secretion of these enzymes in the presence of an obstructed or damaged pancreas may be an important factor in the mortality and morbidity of this disease. It is now generally agreed that the most important controls over enzyme output of the pancreas are the vagus nerves.[3] Hormonal control by secretin elaborated by the duodenum is concerned mainly with the water and bicarbonate content of the external pancreatic secretion.

Theoretically, treatment of the acute phase of the disease could be directed toward operative relief of obstruction of the common or pancreatic duct, or control of pancreatic secretion by vagal inhibition. Experience has shown that operations of any type in the presence of acute pancreatitis carry a higher

This work was supported by United States Public Health Grant (B-52).
Received for publication, Aug. 7, 1951.

mortality than nonoperative forms of treatment.[4] Stomach suction and the use of atropine are measures currently used to control pancreatic enzyme output. A more effective way of accomplishing this control is desirable. An effective parasympatholytic drug should be of definite value in this disease.

The present study is concerned with an evaluation of the influence of the control of pancreatic secretion by a parasympatholytic drug on the course of two varieties of acute experimental pancreatitis in dogs. Banthine, a parasympatholytic drug which has been found to be an inhibitor of pancreatic secretion in animals[5] and man,[6] was used for this purpose.

METHODS

Acute pancreatitis was produced in 50 healthy mongrel dogs as follows: Group I, consisting of 20 animals, had ligation of the main and accessory pancreatic ducts during stimulation of the pancreas with pilocarpine (0.3 mg. per kilogram of body weight) and secretin* (1 μ per kilogram of body weight) given intramuscularly once daily. Ten of these animals were given, in addition, 100 mg. Banthine intramuscularly every six hours. Group II, consisting of 20 animals, had ligation of the main and accessory pancreatic ducts followed by retrograde injection of a 1:1 mixture of bile and trypsin introduced at a pressure of 15 mm. Hg. Likewise, 10 of these animals were treated with Banthine in the manner described above. A control group of 10 animals was subjected to laparotomy with exposure of the pancreatic ducts. All animals were anesthetized with intravenous Sodium Amytal and were given only glucose and saline solution by mouth during the postoperative period. Daily serum amylase determinations were made on all animals, using the method of Huggins and Russell,[7] one amylase unit representing 1 mg. of starch digested in 1 hour. On the fourth postoperative day all surviving animals were sacrificed, necropsy performed, and pathologic sections made of the pancreas.

RESULTS

The variety of pancreatitis produced in Group I animals was relatively nonlethal with only 2 deaths, both occurring in untreated animals. There were no deaths in the Banthine treated group. At necropsy, the pancreas of the untreated group appeared edematous but there was no gross evidence of necrosis. The pancreas of the animals receiving Banthine presented an essentially normal gross appearance. Microscopic section revealed patchy areas of inflammation and mild necrosis in the untreated group. Similar changes were present but much less prominent in the treated animals. The difference in the daily levels of serum amylase is very striking in the treated and in the untreated group (see Fig. 1), the treated animals showing much lower daily values.

In contrast to Group I animals, the variety of pancreatitis occurring in the animals of Group II was a highly fatal type of pancreatic necrosis; 7 of the 10 untreated animals died within 24 to 48 hours, a mortality rate of 70 per cent. The mortality rate of a similar group of animals treated with Banthine was

*Generously supplied by Eli Lilly & Co., Indianapolis, Ind.

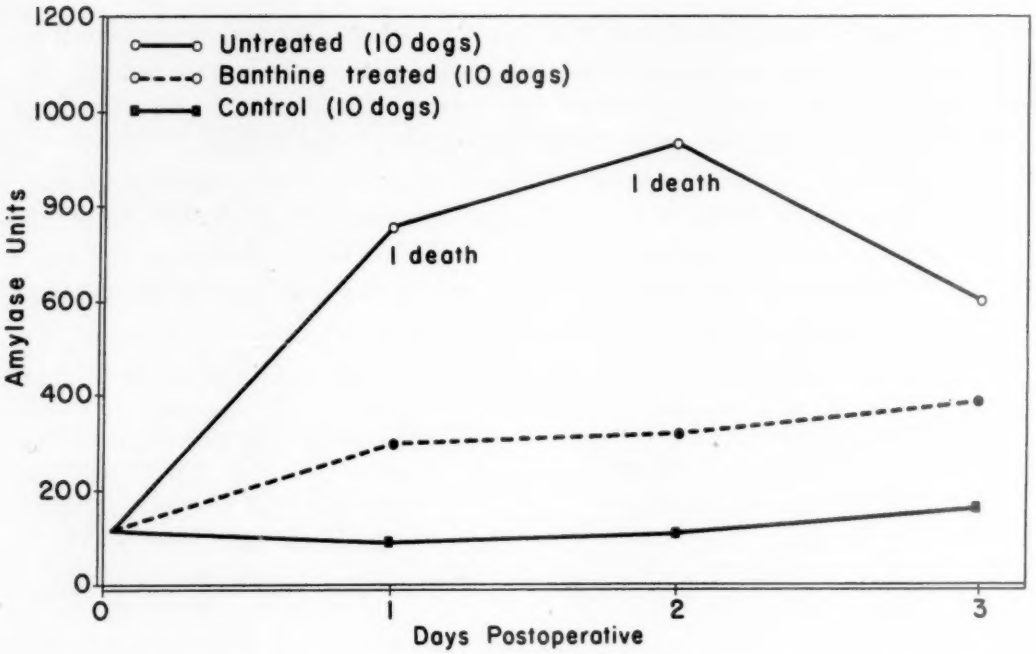


Fig. 1.—This graph shows daily amylase units in dogs having ligation of the pancreatic ducts, followed by daily intramuscular injection of pilocarpine and secretin, resulting in acute edematous pancreatitis in the untreated animals. Control animals had laparotomy with exposure of ducts only.

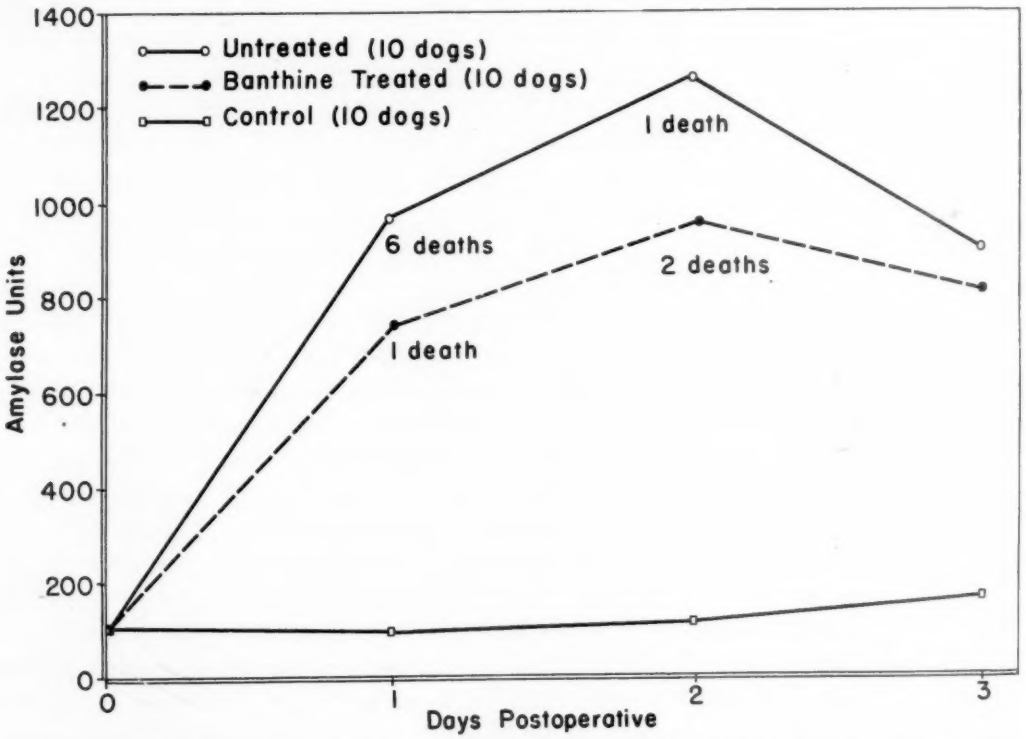


Fig. 2.—This graph shows daily amylase values in the surviving animals after ligation of the pancreatic ducts followed by retrograde injection of bile-trypsin mixture, resulting in acute pancreatic necrosis in the untreated group. The control group had laparotomy with exposure of the ducts only.

reduced to 30 per cent, 3 of 10 dogs dying. Necropsy revealed profound generalized necrosis of the pancreas with surrounding fat necrosis and peritoneal exudate. Pathologic section revealed complete destruction of all pancreatic tissue. Serum amylase determinations in the animals surviving 24 hours, again showed a lower level in the treated group (Fig. 2). A comparison of the survival rate in the treated and untreated groups of animals is shown in Fig. 3.

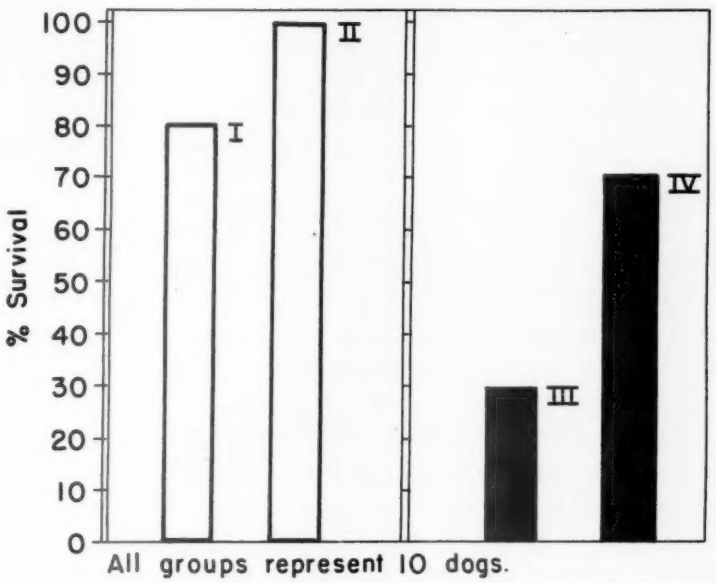


Fig. 3.—*I*, Untreated animals with duct ligation, pilocarpine and secretin injection. *II*, Banthine treated animals with duct ligation, pilocarpine and secretin injection. *III*, Untreated animals with duct ligation and retrograde intraductal bile-trypsin injection. *IV*. Banthine treated animals with duct ligation and retrograde intraductal bile-trypsin injection.

DISCUSSION

Although the etiology of acute pancreatitis is an unsettled issue, the factor of secretion of digestive enzymes in initiating pancreatic injury in the presence of duct obstruction, or of aggravating or potentiating the injury produced by biliary reflux or vascular occlusion, is most important. An effective way of preventing pancreatic enzyme secretion is therefore desirable during an acute episode of pancreatitis. As previously stated, it is now generally recognized that the enzyme secretion of the pancreas is mainly under the control of the vagus nerves. Banthine is an effective agent in reducing resting enzyme output and preventing the enzyme response of the pancreas to various stimuli. A beneficial effect of vagotomy in acute experimental pancreatitis in dogs produced by duct obstruction during stimulation of the gland by feeding has recently been reported by Schaffarzick and co-workers.[8] Ripstein and Thompson[9] have also reported the effect of vagotomy on acute experimental pancreatic necrosis in dogs produced by duct obstruction with retrograde intraductal injection of a bile-trypsin mixture. There was a mortality of 70 per cent in the control group of animals with a reduction of mortality to 30 per cent in the vagotomized animals. These studies indicate a beneficial effect of vagotomy in experimental

acute pancreatitis. The present study adds additional evidence that inhibition of vagal stimulation during the course of acute experimental pancreatitis will lower the mortality and lessen the severity of the disease process.

Chronic recurrent pancreatitis is felt by most observers to be due to repeated acute episodes. These repeated episodes lead to far-advanced damage to the pancreas resulting in severe complications such as pain, diarrhea, malnutrition, and diabetes. If the correct diagnosis were established in the early phases of the disease and subsequent attacks aborted or made less severe by use of a parasympatholytic drug, such as Banthine, these severe complications might possibly be avoided. The effectiveness of this drug in chronic recurrent pancreatitis, however, has yet to be evaluated. McCleery and co-workers[10] have recently reported favorable results in patients having vagotomy for chronic recurrent pancreatitis.

CONCLUSIONS

1. Banthine, a parasympatholytic agent capable of drastically reducing enzyme output of the pancreas, appears to be an effective agent in limiting the severity of acute experimental edematous pancreatitis in dogs, and in reducing the mortality of acute experimental pancreatic necrosis in dogs.

2. This drug should prove of definite value as an adjunct to the current treatment of acute edematous pancreatitis and acute pancreatic necrosis in man, and in other conditions in man where control of pancreatic secretion is desirable, such as duodenal fistula and operations on the pancreas.

3. The beneficial effect of this drug theoretically could be due to inhibition of pancreatic enzyme output by: (1) inhibition of vagal secretory fibers to the pancreas, or (2) reduction of hydrochloric acid output by the stomach, which reduces secretin release by the duodenum, thereby reducing hormonal stimulation to the pancreas. The ability of the drug to overcome spasm of the pancreatic duct or the sphincter of Oddi has yet to be determined.

REFERENCES

1. Lium, R., and Maddock, S.: Etiology of Acute Pancreatitis: An Experimental Study, SURGERY **24**: 593, 1948.
2. Opie, E. L.: The Etiology of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **12**: 182, 1901.
3. Babkin, B. P.: Secretory Mechanism of the Digestive Glands, Ed. 2, New York, 1950, Paul B. Hoeber, p. 840.
4. Morton, J.: Acute Pancreatitis, SURGERY **17**: 475, 1945.
5. Annis, D., and Hallenbeck, G.: The Effect of Banthine on Canine Pancreatic Secretion, Surgical Forum American College of Surgeons, Philadelphia, 1951, W. B. Saunders Company, p. 166.
6. Shingleton, W., Fawcett, B., and Vetter, S.: Pancreatic Secretions and Response to Secretion after Vagotomy and Sympathectomy, Surgical Forum American College of Surgeons, Philadelphia, 1951, W. B. Saunders Company, p. 155.
7. Huggins, C., and Russell, P.: Colorimetric Determination of Amylase, Ann. Surg. **128**: 668, 1948.
8. Schaffarzick, M., Ferran, H., and McCleery, R.: A Study of the Effect of Vagotomy on Experimental Pancreatitis, Surg., Gynec. & Obst. **93**: 9, 1951.
9. Ripstein, C., and Thompson, A.: Acute Pancreatitis: The Influence of the Anatomic Nervous System on the Course of Experimental Pancreatitis, Surgical Forum American College of Surgeons, Philadelphia, 1951, W. B. Saunders Company, p. 161.
10. McCleery, R., Kesterson, J., and Schaffarzick, W.: A Clinical Study of the Effect of Vagotomy on Recurrent Acute Pancreatitis, SURGERY **30**: 130, 1951.

SERUM AMYLASE LEVELS IN EXPERIMENTAL PANCREATITIS

JAMES R. THISTLETHWAITE, M.D., AND ROBERT P. HILL, M.D., WASHINGTON, D. C.

(From the Departments of Surgery and of Pathology, The George Washington University School of Medicine)

ANALYSIS of clinical cases indicates that there is no definite correlation between the degree of elevation of serum amylase and the severity of pancreatitis. It is impossible to determine this accurately on clinical material, for unless a biopsy is taken or there is a fatal outcome, an opportunity to study the pancreas is lacking. In the laboratory an answer to this problem is possible since a pancreatitis of varied intensity may be obtained by utilizing different means of experimental production of the disease. The serum amylase levels can be followed and pathologic examination of the pancreas made at whatever interval is desired. This investigation was undertaken, therefore, to determine whether or not the serum amylase level in the dog will indicate the degree of pancreatitis produced by various experimental methods.

Lium and Maddock,[1] among others, have produced pancreatitis by ligation of the pancreatic ducts. In their report, it was noted that when pancreatic secretion was stimulated by feeding the animal prior to duct ligation, the resultant pancreatitis was more severe than in the fasting animal. Chisholm and Seibel,[2] in their studies of pancreatitis, found that 2 ml. of bile injected into the pancreatic duct would cause pancreatic edema, whereas the introduction of 5 to 10 ml. resulted in pancreatic necrosis.

The pancreatitis resulting from the injection of bile or other substances into the pancreatic duct is thought by many observers to be due to ductal rupture. Rich and Duff[3] have demonstrated ductal rupture from the injection of as little as 2 ml. of India ink into the pancreatic duct by finding particles extruded outside the ductal system. Mann and Giordano[4] noted that the injection of bile into the pancreatic duct under low pressure failed to cause ductal rupture, and, under such circumstances, a true pancreatitis did not develop.

Recently, Popper, Necheles, and Kemper[5] have demonstrated experimentally that edematous pancreatitis can be transformed into hemorrhagic pancreatitis by temporarily occluding the pancreatic arteries. They produced edematous pancreatitis by ligating the pancreatic ducts and stimulating the gland with secretin. When temporary occlusion of the blood supply to the pancreas was added, hemorrhagic pancreatitis resulted.

In the past, the elevation of serum amylase in acute pancreatitis has been attributed to a "spill-over" of this enzyme. According to Janowitz and Hollander,[6] secretion of lipase and amylase occurs not only into the gland lumina (exocrine), but also into the blood stream by way of the tissue spaces (endocrine). They designate this state as the "exocrine-endocrine partition," and add that partition into exocrine and endocrine portions is the normal mode

Received for publication, Aug. 6, 1951.

of secretion of the pancreatic enzymes. In acute pancreatitis then, the increased blood amylase is merely an illustration of the effect of the disease on this physiologic partition.

METHODS OF STUDY

A preliminary experiment was done in order to determine the interval required for maximum amylase response in pancreatitis induced in different ways. Three animals were used. In one, the pancreatic duct was ligated; in another, 3 ml. of bile were injected into the pancreatic duct; and in the third, 3 ml. of saline solution were injected into the pancreatic duct. Daily serum amylase determinations were made after operation on each dog until the levels returned to the preoperative range. Fig. 1 is a graphic representation of the

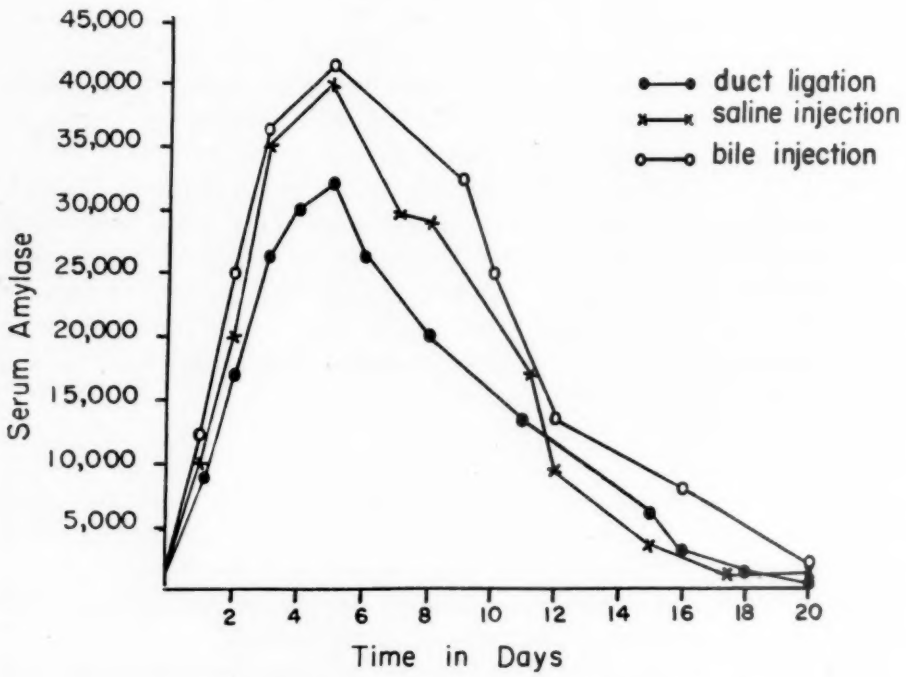


Fig. 1.—Comparison of serum amylase curves.

results obtained. The serum amylase levels increased correspondingly in each animal, reaching their peak between the second and fifth postoperative days, but remaining elevated slightly longer in the dog having had the injection of bile. The serum amylase returned to normal levels in all three dogs between the eighteenth and twentieth postoperative days. From this study it was decided to sacrifice the animals in future experiments on the second, third, or sometimes fourth postoperative day so that pathologic examination could be made when the serum amylase was still rapidly rising and approaching its maximum.

Mongrel dogs of both sexes, weighing from 6 to 12 kilograms, were used. All were anesthetized with intravenous Nembutal, and the operations were per-

formed under aseptic conditions. In those dogs having duct ligation, care was taken in each instance to ligate both ducts. When stimulation of the vagus nerves was done, faradic current was applied to the intact cervical trunks.

The animals were divided into 5 groups according to the procedures selected for study: (1) ligation of the pancreatic ducts in fasting and nonfasting animals, duct ligation followed by vagal nerve stimulation, duct ligation and vagus nerve stimulation combined with arterial occlusion, (2) injection of an irritant into the ducts, (3) injection of a nonirritant into the ducts, (4) chemical pancreatic trauma, and (5) mechanical pancreatic trauma.

Serum amylase determinations were made at 24, 48, 72, and sometimes 96 hours in all groups. Determinations were made according to the method of Smith and Roe.[7] It should be remembered that a dog's normal amylase level is about 10 times that of man. Control fasting levels ranged between 475 and 850 units per 100 ml. of serum.

All animals were sacrificed on the second, third, or fourth postoperative day and gross pathologic changes noted. Several sections were taken from each pancreas and fixed in 10 per cent formalin.

The degree of microscopic change was arbitrarily divided into 3 categories.

Grade 1: Minimal to moderate edema of the interlobular septa with slight diffuse acute inflammatory reaction in the septa, infrequent small areas of fat necrosis, no significant glandular destruction, minimal areas of intralobular edema.

Grade 2: Similar changes as Grade 1 with more severe inflammatory reaction, and more frequent areas of fat necrosis, areas of hemorrhage in the septa, small foci of glandular necrosis.

Grade 3: More pronounced changes than Grade 2 with frequent areas of fat and glandular necrosis, beginning replacement fibrosis of destroyed glandular tissue in the later stages.

This classification is not based on the presence or absence of any particular lesion, but on the degree and diffuseness of the changes present. Examples of certain specific focal lesions are illustrated in Fig. 2.

RESULTS

Group 1, Ligation of the Pancreatic Ducts.—Three variants of this method were utilized: (a) These animals were run simultaneously in pairs, 1 pair having been fasted and the other having been fed 2 hours prior to ligation. In all animals the serum amylase increased to about 30,000 units in 72 hours. There were no remarkable gross pathologic findings in either series when the dogs were sacrificed. Microscopic changes in the pancreases were classified as Grade 1.

(b) Vagal nerve stimulation with faradic current was used to promote pancreatic secretion in 3 dogs after the ducts had been ligated. This resulted in an obvious edema of the pancreas observed while the abdomen was still open.

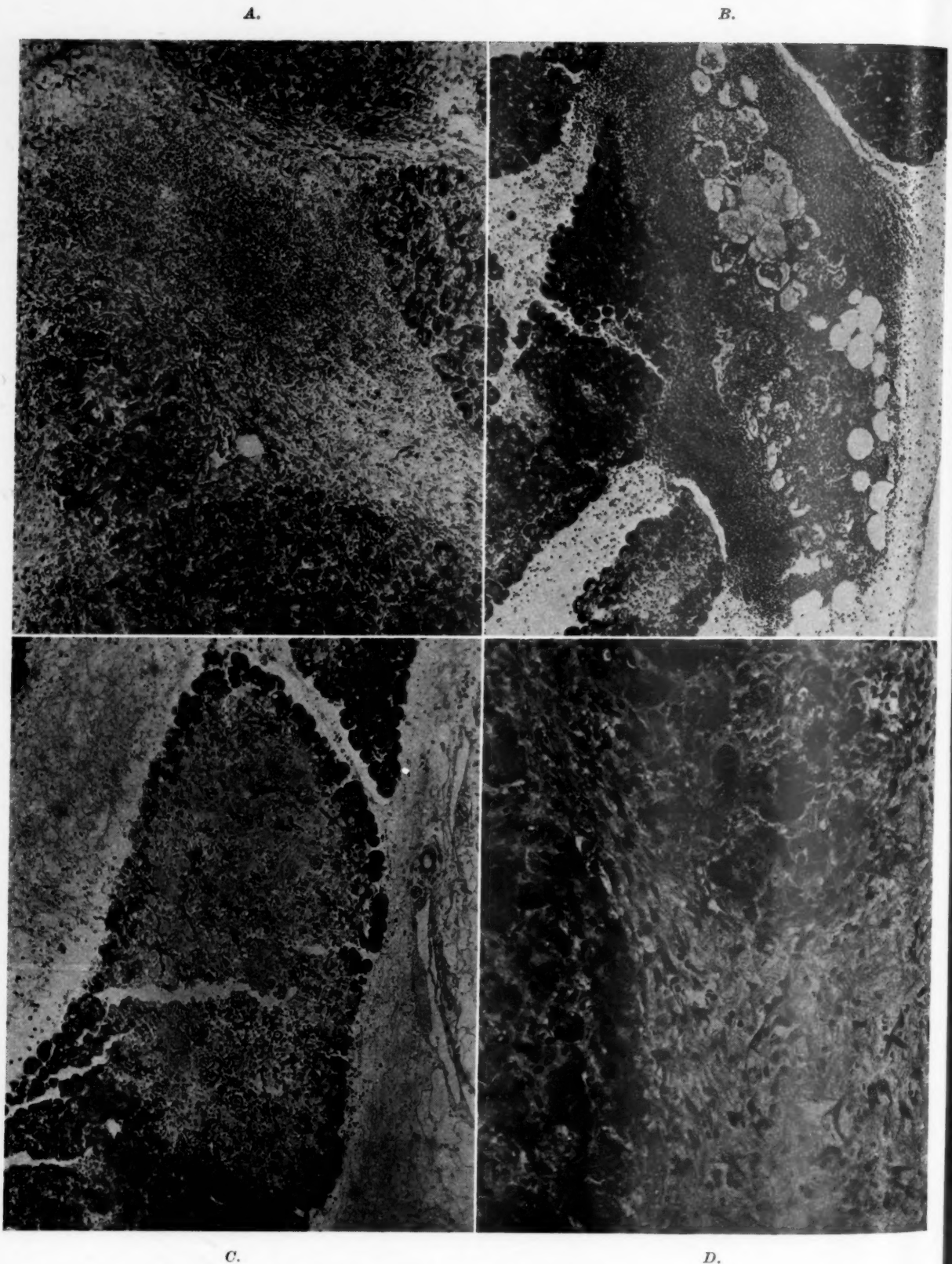


Fig. 2.—*A*, Changes in the pancreas 48 hours after ligation of the pancreatic ducts. Note the prominent edema, inflammatory cell infiltration, and fibrin deposition in the interlobular fibrous tissue. The acini are also separated by edema. In this particular field, the changes are more severe than elsewhere in the pancreas. Grade 1.

B, Changes in the pancreas 48 hours after injection of bile into the pancreatic duct. Focal necrosis is apparent in one lobule near the lower edge. Fat necrosis, edema, and acute inflammatory cell infiltration are present. Grade 2.

C, A focus of necrosis in a pancreatic lobule 48 hours after injection of bile into the pancreatic duct. The interlobular fibrous tissue is edematous and contains a fibrinous exudate. Grade 3.

D, A pancreatic lobule being replaced by fibroblasts 72 hours after injection of bile into the pancreatic duct. Grade 3.

In these animals the serum amylase rose to the same levels as when duct ligation alone had been done. Microscopic examination of the pancreases 48 and 72 hours after operation revealed Grade 1 changes.

In a separate experiment it had been determined that nerve stimulation alone produced no appreciable pathologic changes in the pancreas. Serum amylase determinations made hourly for the first 6 hours showed a maximum increase of 400 units in 1 of 3 animals, a negligible response considering the high elevations attained by other methods.

(c) The vagus nerves were stimulated in 3 dogs after the pancreatic ducts had been ligated, and, in addition, the pancreatic arteries were completely occluded for 15 minutes. The serum amylase levels were only slightly higher in this group, averaging 33,000 units after 72 hours. However, when these animals were examined, 2 of the 3 had blood-tinged fluid in their peritoneal cavities, and fat necrosis was evident in the omentum and the pancreas. Microscopically, the changes in the pancreases were classified as Grade 2.

Group 2, Injection of an Irritant Into the Pancreatic Duct.—Three milliliters of bile were aspirated from the gall bladder and injected slowly into the major pancreatic ducts of 4 dogs. This produced immediate interlobular edema of the pancreas in most instances. At 72 hours, peak levels of serum amylase were between 35,000 and 40,000 units. When these animals were killed, 200 to 300 ml. of blood-tinged fluid were present in the peritoneal cavity. There were also areas of fat necrosis in the omentum and pancreas. The pancreases showed Grades 2 and 3 changes when examined microscopically.

Group 3, Injection of a Nonirritant Into the Pancreatic Duct.—For this series, 3 to 5 ml. of physiologic saline solution were injected into the ducts of 4 animals. This frequently produced interlobular edema of the pancreas a few minutes after injection. The serum amylase rose to about 35,000 units 72 hours later. When these animals were sacrificed, there were no gross pathologic changes. Microscopic findings in the pancreases were classified as Grade 1.

Group 4, Chemical Pancreatic Trauma.—Three milliliters of bile were injected into the substance of the pancreas rather than into the pancreatic duct. There was no significant rise in the serum amylase. When these 3 animals were killed, an interlobular edema was evident at the injection sites on gross examination. Microscopically, the pancreases showed considerable interlobular edema, mild inflammatory cell infiltration and small foci of fat necrosis at the injection sites. An occasional gland along the periphery of the lobules was destroyed. There were no changes in other regions of the pancreas.

Group 5, Local Mechanical Pancreatic Trauma.—The pancreases of 3 dogs were crushed with a clamp, care being taken not to injure a major duct. This failed to cause an elevation in the serum amylase, and the pancreases were normal on microscopic examination except for minimal inflammatory reaction and necrosis in the areas where the lobules had been crushed.

Table I is a summation of the methods used and the results obtained.

TABLE I

	METHOD	SERUM AMYLASE LEVELS	GRADE OF PATHOLOGIC LEVELS
Group 1	(a) Duct ligation alone	30,000	1
	(b) Duct ligation, stimulation of secretion	30,000	1
	(c) Duct ligation, stimulation of secretion, arterial occlusion	33,000	2
Group 2	Bile injection into ducts	35,000	2 and 3
Group 3	Saline injection into ducts	35,000	1
Group 4	Bile injection into pancreas	Normal	0
Group 5	Crushing of pancreatic substance	Normal	0

DISCUSSION

Comparison of these results indicates that there is little difference in the pathologic lesions in the pancreas when the ducts are ligated in a fasting animal and when they are ligated after pancreatic secretion has been promoted by feeding or by vagal stimulation, although Lium and Maddock, as previously indicated, believed that the pancreatitis was somewhat more severe when the animal had been fed. Approximately the same degree of pancreatitis resulted from the injection of saline solution into the ductal system. However, when bile was used, or the arterial supply temporarily occluded following duct ligation, the pancreatitis was much more pronounced. Nevertheless, regardless of the severity of the pancreatitis, the serum amylase increased to approximately the same levels indicating little significant correlation between the two. However, there was a slightly earlier rise in the amylase in those cases showing Grades 2 and 3 changes.

Our findings that the serum amylase increased correspondingly when a similar amount of bile or saline solution was injected into the pancreatic duct may be explained by ductal rupture with resultant pancreatitis and disturbance of the exocrine-endocrine partition of the enzymes. The explanation for the difference in the degree of pancreatitis, however, still remains obscure. The production of hemorrhagic pancreatitis by duct ligation followed by interruption of the vascular supply, observed by Popper and associates and supported in this study, may afford a clue.

Bile possesses certain irritating properties since it has been shown, for instance, that concentrated bile injected into the pancreatic duct will cause a more pronounced pancreatitis than will dilute bile.[8] Also it is well known that bile causes a pronounced inflammatory response in tissues to which it is foreign as, for example, the peritoneum. Therefore, although ductal rupture occurs when either bile or saline solution is injected, the more marked pancreatitis following the use of bile may be due to its local irritant effect causing vasospasm in focal areas. This, then, may lead to tissue anoxia in these areas and render them more susceptible to the necrotizing action of the pancreatic enzymes.

The failure of bile to cause a true pancreatitis when injected only into the substance of the pancreas is in conformity with the concept that ductal rupture with release of pancreatic enzymes is the most important factor in the development of experimental pancreatitis. The tissue changes at the injection site

were similar to those observed by Mann and Giordano throughout the pancreas when bile was injected into the ducts without disruption of the ductal system, namely, an interlobular edema without significant alteration in the glandular substance. Under such circumstances, the serum amylase levels would be expected to remain within normal limits as was indeed the case. A somewhat analogous situation exists when the pancreas is subjected to local mechanical trauma without injury to the ducts.

It is of interest that the most pronounced degree of pathologic change in the pancreas was manifested at 48 hours. When the serum amylase was at its peak at 72 hours, the acute inflammatory reaction was beginning to subside and replacement fibrosis was starting in those cases in which destruction of pancreatic substance had taken place.

SUMMARY

Serum amylase is elevated markedly when the pancreatic ducts are ligated, or when substances are injected into the pancreatic ducts.

Serum amylase is not elevated when pancreatic trauma is produced without injuring the ductal system.

Comparison of the pancreatitis produced by various experimental methods shows little significant correlation between the degree of elevation of the serum amylase and the severity of the pancreatitis.

REFERENCES

1. Lium, R., and Maddock, S.: Etiology of Acute Pancreatitis, SURGERY **24**: 593, 1948.
2. Chisholm, T. C., and Seibel, R. E.: Acute Pancreatitis. II. An Experimental Study With Special Reference to X-Ray Therapy, Surg., Gynec. & Obst. **85**: 794, 1947.
3. Rich, A. R., and Duff, L. G.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **58**: 212, 1936.
4. Mann, F. C., and Giordano, A. S.: The Bile Factor in Pancreatitis, Arch. Surg. **6**: 1, 1923.
5. Popper, H. L., Necheles, H., and Kemper, C.: Transition of Pancreatic Edema Into Pancreatic Necrosis, Surg., Gynec. & Obst. **39**: 79, 1948.
6. Janowitz, H. D., and Hollander, F.: The Exocrine-Endocrine partition of enzymes in the digestive tract, Gastroenterology **17**: 591, 1951.
7. Smith, B. W., and Roe, J. H.: A Photometric Method for the Determination of Amylase in Blood and Urine, With Use of the Starch-Iodine Color, J. Biol. Chem. **179**: 53, 1949.
8. Flexner, S.: The Constituent of the Bile Causing Pancreatitis and the Effect of Colloids Upon Its Action, J. Exper. Med. **8**: 167, 1906.

RENOGASTROEPIPLOIC ANASTOMOSIS IN THE TREATMENT OF PORTAL HYPERTENSION

RAYMUNDO DE BRITTO,* OCTAVIO VAZ,* PEDRO ABDALLA,* AND RODRIGUES DA SILVA,** RIO DE JANEIRO, BRAZIL

THE venous shunt operations of the portacaval type are, without any doubt, the most rational, efficient, and revolutionary therapeutic method tried up to now in the treatment of portal hypertension. According to Pateck, quoted by Blakemore, even under proper medical-dietetic treatment, 34 per cent of the patients with hepatic cirrhosis are assailed by digestive hemorrhages and 50 per cent do not survive the first year of the disease because of these complications.

In order to correct these disturbances, many therapeutic methods have been suggested and put into practice, but in general, they proved to be inefficient, with exception of the favorable cases. Thus, the results obtained are somewhat vague and of temporary duration.

One decisive step in solving the problem was taken by Blakemore and collaborators of the Spleen Clinic of the Presbyterian Hospital, New York. This group of surgeons, after thorough studies, based on clinical, surgical, and experimental facts, was able to do successfully the anastomosis of the vena porta with the inferior vena cava, by means of vitallium tubes.

New progress in the solution of the problem was obtained by modifying the original procedure. The left splenorenal shunt, with replacement of the vitallium tube by methods of direct venous sutures, was used with success by many surgeons, initially with nephrectomy and afterward with preservation of the kidney. Even the direct side-to-side portacaval anastomosis could be performed, thus avoiding a serious inconvenience of the primary method—the suppression of the circulation to the liver.

At the present, about 200 operations of this type have been published by several authors: Blakemore (111 cases), Linton (44 cases), Julian and Fildes (18 cases), Mulligan (16 cases), Walsh and Callow (14 cases), Santy and Marion (8 cases) and others with fewer cases. There have been some operations of this type in Brazil but unfortunately they have not been published.

The practical results with these types of portacaval anastomoses cannot yet be properly appreciated, particularly because a longer period of observation and analysis of the cases in which operations have already been performed is necessary. However, they point to a more brilliant perspective, due to a better technique and to the knowledge of new facts related to the pathology of portal hypertension.

In this presentation, the authors describe their personal experience based on 3 patients with portal hypertension who were subjected to venous shunt operations in the Hospital dos Servidores do Estado. In one of the cases, an anastomosis between the right gastroepiploic vein and the left renal vein was

Received for publication, Aug. 24, 1951.

*From the Department of General Surgery, Hospital dos Servidores do Estado.
**From the Department of Internal Medicine, Hospital dos Servidores do Estado.

performed, which we believe is the first time the venous circle of the greater curvature of the stomach has been used for this type of surgery. In the other two cases, a splenorenal anastomosis was performed. The kidney was preserved in all three cases.

The clinical history of the case in which an anastomosis between the gastroepiploic vein and the left renal vein was carried out is here summarized.

CASE REPORT

P. P. M. (98,394), a 35-year-old white man, was admitted on June 1, 1951. A splenorenal anastomosis was suggested. The patient gave a history of hematemesis followed by melena, two months previous to admission. Two years before that, *Schistosoma mansoni* eggs had been found in the feces and he was submitted to stibiotherapy. Four years before admission he had been treated with Aralen Diphosphate because malaria was suspected. About three years prior to the Aralen treatment he had been operated on for acute suppurative appendicitis.

Physical examination showed a palpable spleen, three fingerbreadths below the edge of the ribs, with diminished consistence, which was painless and movable. Liver was palpable a little below the costal edge, at the level of the epigastrium, apparently without alteration of consistence or sensibility.

X-ray examination of the esophagus showed varicose veins in the lower third of the organ.

Proctosigmoidoscopy showed granulous and congested mucosa, with huge dilatations corresponding to veins of the submucosa from the anorectal line to the first Houston valve.

Other findings were: intradermic reaction with antigen of *Schistosoma mansoni*—positive, rectal biopsy—negative concerning *Schistosoma mansoni* eggs, blood count: red blood cells—4,240,000, hemoglobin—82 per cent, leukocytes—4,500 with 49 per cent segmented neutrophils, 11 per cent nonsegmented, 36 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophils, 0 per cent basophils, platelets, 210,000.

Liver function tests showed cephalin-cholesterol flocculation to be negative, thymol flocculation negative, thymol turbidity 2 units and bromsulfalein retention 0 per cent in 20 minutes. Excretion of hippuric acid (venous method): 1.03 Gm. total serum proteins: 7.5 per cent with 5.4 Gm. per cent albumin and 2.1 per cent globulin.

Puncture biopsy of the liver showed that the hepatic framework was well preserved, cytoplasm of some cells clear and granulous.

A diagnosis of portal hypertension probably due to subhepatic obstruction (portal-vein) was established.

Operation was performed on June 6, 1951: splenectomy and anastomosis of the right gastroepiploic vein to the left renal vein. This procedure was determined by the finding of a complete thrombosis of the splenic vein, the hylar inferior branch of which was free, very large, and in continuation with the right gastroepiploic vein. The venous blood of the spleen discharged mostly through this great and uniform channel, with a diameter the size of a little finger, going to the portal vein. The venous pressure in this channel dropped from 270 mm. of water before the anastomosis to 232 afterwards. The possibility of another venous obstruction was considered, probably of the portal vein, for other veins that could be seen as left gastric and inferior mesenteric veins were also enlarged. The hypothesis of a cirrhotic liver was discarded, for two biopsies done during the operation showed no hepatic alterations of that type.

The patient was out of bed and in good condition on the fiftieth postoperative day.

TECHNIQUE

In all the cases, the principles of Linton's method, as explained in *Surgical Clinics of North America*, October, 1947, were adopted.

The procedure was as follows: thoracoabdominal incision from the posterior axillar line to the abdominal midline, access through the ninth intercostal space, opening of the pleural and peritoneal cavities, incision of the anterior portion of the diaphragm parallel to the cutaneous wound, retraction of the spleen forward, division of the lienorenal, phrenocolic, and gastrolienal ligaments, ligature of the vasa brevia, and division and ligature of the splenic artery.

In dissecting the splenic pedicle we could see a complete thrombosis of the splenic vein, which was reduced to a simple fibrous cord. This thrombotic process reached the upper hilar branch and the lower hilar branch up to the level where it received the left gastroepiploic vein. This vein, extremely dilated, had the caliber of a little finger and was in perfect continuity with the right one. Accordingly, the venous circle of the greater curvature of the stomach resulted in a uniform channel from the spleen to the portal vein. The venous blood of the spleen was emptied by this channel.

After removal of the spleen, the venous pressure of the gastroepiploic vein was measured. We used Cohen's manometer* and found the pressure to be 270 mm. of water. It was obvious that the channel mentioned previously was a supplementary path to the splenic vein. It was hypertensive and this fact together with the huge dilatations of all the portal system veins indicated the existence of another obstruction, perhaps in the portal vein itself.

We were faced with a peculiar situation and had to make a prompt decision. It was not only a technical problem. One of two procedures could be followed: a simple splenectomy or a portarenal anastomosis. The first way was not justified since thrombosis was not limited to the splenic vein. The second way was correct and in this case we chose a tributary of the portal vein. We preferred the gastroepiploic vein, for several reasons: its easy handling, its good caliber, its function as substitute for the splenic vein, its connection with the veins of the lesser curvature of the stomach and lower esophageal veins by means of the prepyloric vein of Mayo (Fig. 1).

Inasmuch as we decided to use the gastroepiploic channel we isolated it up to the duodenum and divided it at the level where the vertical and horizontal portions of the stomach joined. The gastroepiploic vein was occluded with a Potts ductus clamp and then anastomosed to the renal vein (Fig. 2). The pancreas had a low situation, which made the technique easier and prevented exaggerated angulation of the vein.

The venous pressure in the right gastroepiploic vein, after the shunt, lowered to 232 mm. of water, which proved the correctness of our procedure. At the same time we could observe complete collapse of the lower esophageal veins and those of the lesser curvature of the stomach.

The peritoneum was incised over the kidney and this organ mobilized. The renal artery was isolated and clamped with a small bulldog clamp so that arterial inflow to the kidney during venous anastomosis was prevented. Sufficient length of the renal vein was dissected to allow application of two clamps with a space of 4 cm. between them. We must always remember that for

*Made by Becton, Dickinson and Company.

anatomic and embryologic reasons, the left renal vein presents more anatomic variation than the right one. It receives the genital and adrenal veins which greatly disturb the dissection of the pedicle. Anastomosis between the end of the gastroepiploic vein and the anterosuperior surface of the renal vein was done. This was accomplished in about 30 minutes. A transverse incision in the renal vein in a length equal to the diameter of the gastroepiploic vein was made. Continuous anterior and posterior sutures of the intima-to-intima type with stay sutures in the angles, all 00000 Deknatel silk, were used.

The clamps on the veins were removed first, the hemostasis was verified and the clamp on the renal artery was removed afterward.

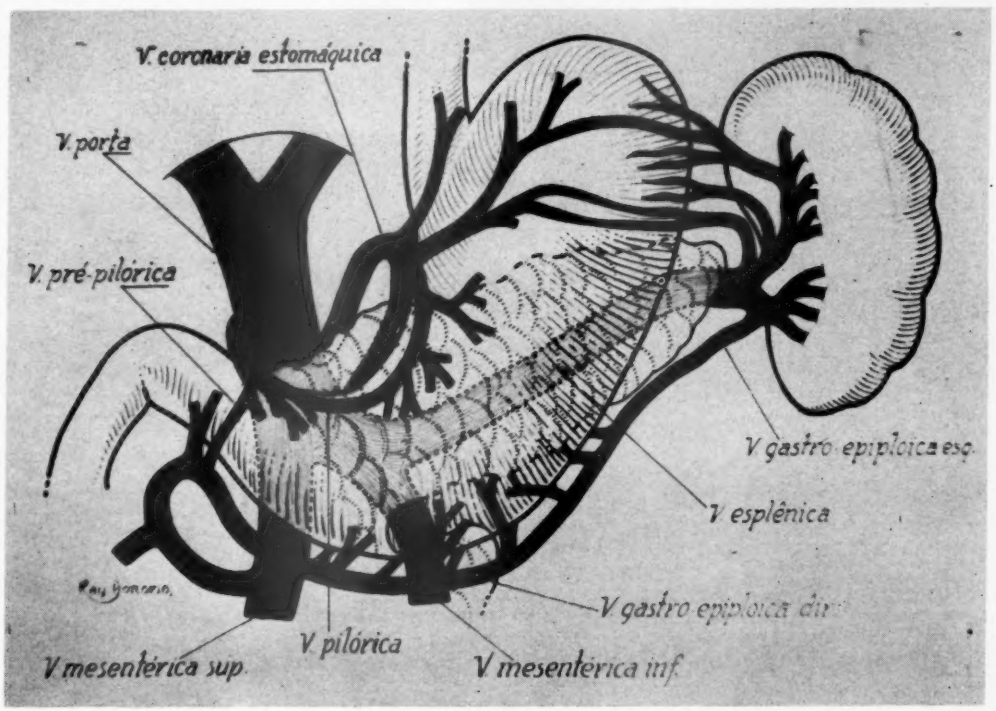


Fig. 1.—This picture shows the venous circulation to the portal vein. Prepyloric vein of Mayo is emphasized in order to point out the connection between the venous circles of the lesser and greater curvatures of the stomach.

The kidney was replaced in its fossa and the peritoneum sutured over it. The diaphragm and thoracoabdominal incision were closed in layers. The pleural cavity was drained by a rubber tube of the Pezzer type.

After closure of the posterior parietal peritoneum, the greater omentum was sutured to the greater curvature of the stomach in order to close the gastroepiploic opening and prevent possible internal hernias (Fig. 3).

In view of the traumatic aspect and long time required by this operation, about 7 hours, we used an abundant volume of blood, sometimes injected under pressure.

General anesthesia, in closed circuit with tracheal intubation, was employed. Nembutal, nitrous oxide-oxygen, curare, and oxygen were the anesthetic agents preferred.

COMMENT

We believe that the end-to-side splenorenal shunt through thoracoabdominal incision is much more advantageous than direct portacaval anastomosis, for physiopathologic and technical reasons.

The following are the essential aspects that give it practical value:

1. It produces a partial shunt of the portal blood flow so that the liver is not completely by-passed. Some blood enters the liver which is in accordance with the functional and anatomic requirements of this organ.

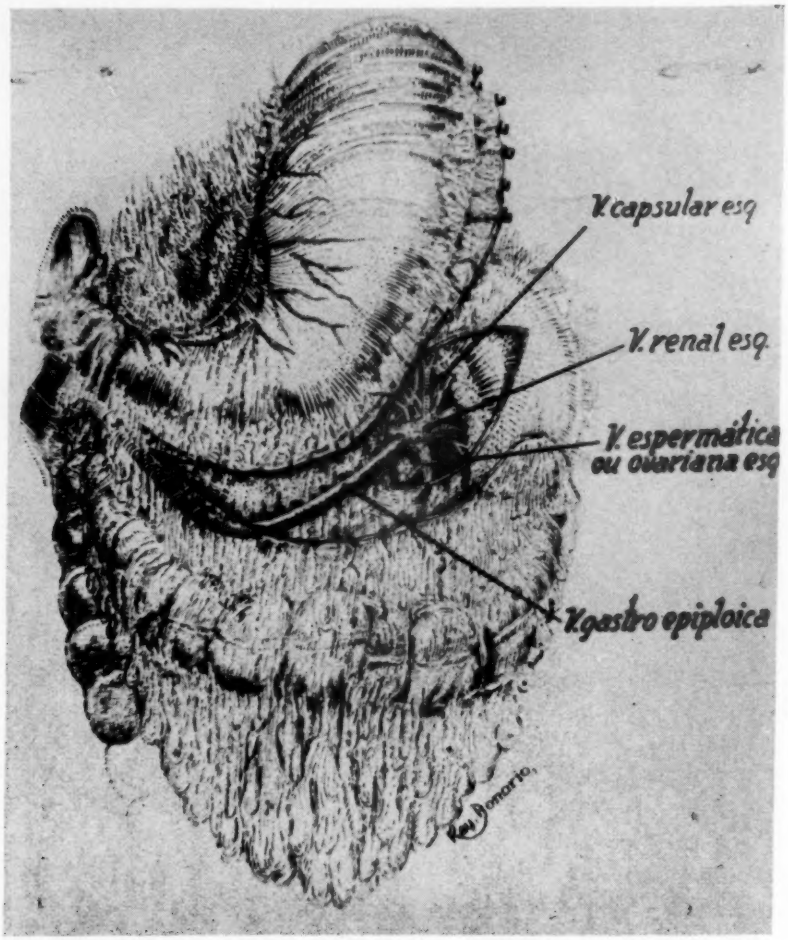


Fig. 2.—The anastomosis between the right gastroepiploic vein and the left renal vein.

2. The splenorenal shunt reduces portal hypertension satisfactorily, since about 50 per cent of the portal blood may go through the renal vein. Linton registers tensional falls from 400 mm. to 200 mm. of water after the anastomosis.

3. In end-to-side splenorenal shunt the kidney is not sacrificed. Preservation of this organ is in some cases of the utmost importance.

4. The splenorenal shunt allows subsequent direct portacaval anastomosis, should this become necessary.

5. The splenorenal shunt may be performed in cases of either intrahepatic or extrahepatic obstruction, which is not feasible with direct portacaval anastomosis.

6. Splenectomy aids in lowering portal tension since it reduces the arterial flow to the portal area by about 40 per cent.

7. Splenectomy leads to division of many collateral channels which feed esophageal varices.

8. Splenectomy promotes immediate cure of hypersplenism, which does not occur as satisfactorily with direct portacaval shunt, as recognized by Blakemore.

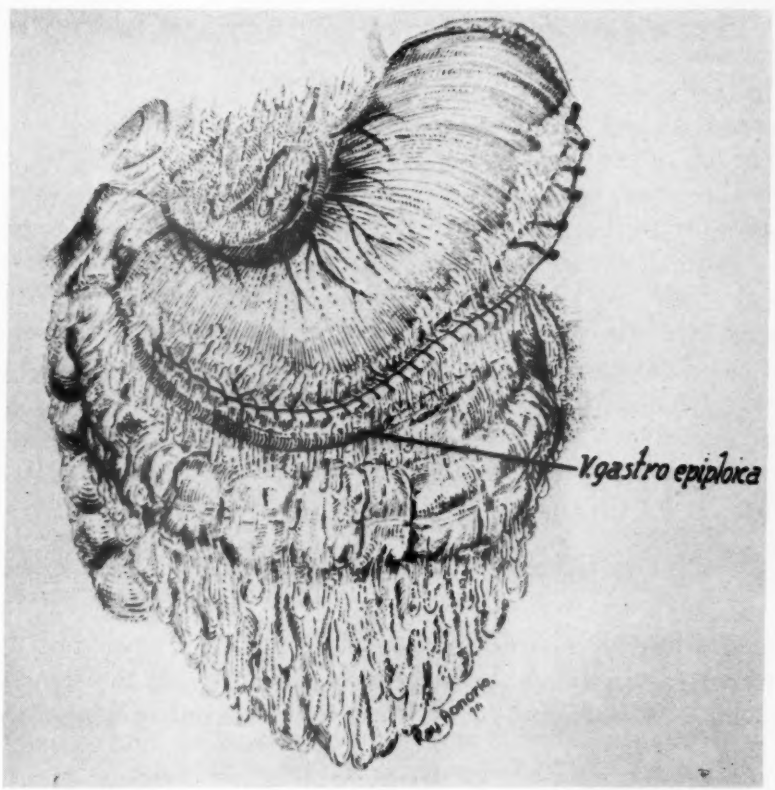


Fig. 3.—This picture shows the end result of the renogastroepiploic shunt after closure of the gastrocolic opening.

9. End-to-side anastomosis is less thrombogenic, due to suction of the blood from the splenic vein by the circulatory flow in the renal vein, as Blalock has demonstrated. Linton considers that this is true, for he has never observed thrombosis in his cases.

10. Thoracoabdominal approach is of great practical value. There are no vital structures in the region of approach. It offers an excellent exposure of the spleen and kidney and their vessels. Surgery of the upper left abdomen in the opinion of Léger and Patel is easier and better tolerated than the dis-

section of a richly vascularized hepatic pedicle. These are the reasons why the thoracoabdominal approach must be considered very good, as it aids in reducing technical difficulties and in creating more favorable conditions for the surgeon's work.

Some technical points which we believe to be essential should be emphasized:

1. The anastomotic opening should not be narrow. Anterior and posterior continuous sutures must be fixed to stay sutures in the angles. If the splenic vein caliber is too large, interruption at three points is advised.

2. The renal vein has to be isolated in a sufficient length so that the distance between the clamps provides space enough for good anastomosis.

3. It is absolutely necessary that the cut edges of the vein walls be everted so that intima is approximated to intima.

This type of suture warrants a resistant anastomotic opening, a strong scar, a good hemostasis and, much more important than everything else, little tendency to thrombosis.

4. Adventicectomy of the edges of the vein walls should not be forgotten.

5. Occlusion of the renal artery must be limited to 35 minutes. Prolonged ischemia is deleterious to the kidney.

6. Dissection of the renal pedicle must be done carefully in order not to damage the vessels. Preservation of the kidney is the basic characteristic of the method.

Splenorenal anastomosis is sometimes impractable or insufficient. This happens in cases in which (1) the splenic vein is too narrow because of a slight splenomegaly (common in hepatic cirrhosis),

(2) the splenic vein is stenosed or thrombosed, making the shunt useless, unless the left gastric vein is under the influence of the obstruction or unless there is thrombosis of the portal vein (a case of this last type is reported here), and

(3) there was previous splenectomy or there are local technical difficulties (hypervascularization, adherences).

Linton and Rousselot stress that splenectomy must never te tried in cases of portal hypertension unless the surgeon is perfectly able to perform a splenorenal anastomosis which many times can be indicated only during the operation.

POSTOPERATIVE CARE

Careful observation of the patient is required during the early postoperative period, especially for the first 48 hours, a critical period when many complications may occur. Postoperative treatment that should be emphasized in this type of surgery includes: maintenance of the normal level of fluids, proteins, vitamins, and mineral salts in the blood, and prevention of cardiovascular disturbances.

Blood pressure is measured at frequent intervals to detect early symptoms of shock.

The patient is encouraged to start moving the lower limbs as soon as possible to avoid venous thrombosis.

We prescribe inhalation of carbogene and breathing exercises, and we encourage the patient to cough, in order to prevent pulmonary complications.

It is very important to relieve pain by sedation so that the patient can breathe deeply. This also helps to prevent pulmonary complications.

Since abdominal distention may lead to compression of veins and thereby to venous thrombosis, it may be prevented by means of continuous gastric suction. A Levine tube is used for the first 48 hours and its use prolonged if necessary.

Antibiotics are prescribed prophylactically, especially penicillin and streptomycin.

Fig. 4. Fig. 5.

Fig. 4.—Varicose veins of the lower third of the esophagus as seen before the operation.
Fig. 5.—X-ray film of the esophagus one month after the operation.

Thrombosis and heparinization present a very difficult problem. Thrombosis is the prime cause of surgical failure. If it supervenes it always does so early in the postoperative course. Since thrombosis always occurs early heparin would have to be used early, but the possibility of severe bleeding does not justify, in our opinion, the prophylactic use of this anticoagulant.

Occlusion of the renal vein up to 35 minutes is not disturbing to the kidney since the renal artery is also occluded. Failure to clamp the artery is likely to cause hemorrhagic infarction as has been demonstrated by Blalock and Johns. Recently, Adams has said that according to experiments ischemia is more dangerous to the kidney than congestion and suggests that the occlusion of the renal artery during the anastomosis is not to be advised. He thinks that the ideal method consists of lateral clamping of the renal vein so that the circulation to the organ is not disturbed. We agree with this.

Cirrhotic patients are likely to develop prompt hepatic failure. A proper diet is essential and must be followed both in the preoperative and in the postoperative course.

Acute necrosis of the pancreas is an infrequent, but terrible complication. In order to prevent it we are careful in handling the pancreas and we do not resect its tail unless forced to do so.

SUMMARY

The authors report three cases of portacaval shunt in the treatment of portal hypertension, with special reference to one case in which an anastomosis between a very dilated right gastroepiploic vein and a left renal vein was performed (Fig. 2). In this patient liver function tests were good and hepatic biopsies showed no fibrosis. Hypersplenism was present. The kidney was preserved. He was alive and well one and one-half months after the operation.

The patient showed complete regression of the esophageal varicose veins and absence of any other hemorrhagic episode (Figs. 4 and 5).

REFERENCES

1. Adams, H. D.: Treatment of Portal Hypertension and Associated Acute Hemorrhage, S. Clin. North America **31**: 803-812, 1951.
2. Blakemore, A. H.: Portacaval Shunt in Surgical Treatment of Portal Hypertension, Ann. Surg. **128**: 825-842, 1948.
3. Blakemore, A. H.: Portacaval Anastomosis, Observations on Technic and Postoperative Care, S. Clin. North America **28**: 278, 1948.
4. Blakemore, A. H.: Portacaval Shunt for Portal Hypertension, J. A. M. A. **145**: 1335-1339, 1951.
5. Blalock, A.: The Use of Shunt or By-Pass Operations in the Treatment of Certain Circulatory Disorders, Including Portal Hypertension and Pulmonic Stenosis, Ann. Surg. **125**: 129, 1947.
6. Julian, O. C., and Fildes, C. E.: Shunt Operation for Esophageal Varices, S. Clin. North America **31**: 229, 1951.
7. Linton, R. R., Jones, C. M., and Volwiler, W.: Portal Hypertension, Treatment by Splenectomy and Splenorenal Anastomosis With Preservation of Kidney, S. Clin. North America **27**: 1162-1170, 1947.
8. Linton, R. R.: Portacaval Shunts in Treatment of Portal Hypertension, Special Reference to Patients Previously Operated on, New England J. Med. **238**: 723-727, 1948.
9. Linton, R. R., Hardy, J. I. B., and Volwiler, W.: Portacaval Shunts on Treatment of Portal Hypertension, Analysis of 15 Cases With Special Reference to Suture Type of End-to-Side Splenorenal Anastomosis With Splenectomy and Preservation of Kidney, Surg., Gynec. & Obst. **87**: 129-144, 1948.
10. Linton, R. R.: The Surgical Treatment of Bleeding Esophageal Varices by Portal Systemic Venous Shunts With Report of 34 Cases, Ann. Int. Med. **31**: 5,794, 1949.
11. Lord, J. W., Jr.: The Surgical Management of Secondary Hypersplenism, SURGERY **29**: 407-418, 1951.
12. Martinet, J. D., and Tubiana, R.: Pathologie des Veines, Paris, 1950, Gaston Doin & Cie.
13. Mulligan, L. V.: Venous Shunts in Portal Hypertension, S. Clin. North America **30**: 1,465, 1950.
14. Patel, J., and Léger: Cited by Martinet and Tubiana.[12]
15. Rousselot, L. M.: Combined (Onestage) Splenectomy and Portacaval Shunts in Portal Hypertension, Observation on Venous Shunts in Postsplenectomy Patient With Recurring Hemorrhage, J. A. M. A. **140**: 282-286, 1949.
16. Santy, P., and Marion, P.: Traitement de l'hypertension portale par derivation porto-cave (8 cas), Acta chir. belg. **22**: 550, 1949.
17. Walsh, C. S., and Callow, A. D.: An Appraisal of Current Methods for the Treatment of Portal Hypertension, Rev. Gastroenterol. **17**: 423, 1950.

AN EXPERIMENTAL STUDY OF PROTEIN AND FAT ASSIMILATION AFTER TOTAL GASTRECTOMY

TILDEN C. EVERSON, M.D., PH.D., CHICAGO, ILL.

WITH THE TECHNICAL ASSISTANCE OF EVERETT HOPPE

(From the Department of Surgery, College of Medicine, University of Illinois)

IN RECENT years there has been increasing application of the procedure of total gastrectomy in the surgical treatment of gastric cancer. The more frequent utilization of this operation makes mandatory an appraisal of the ability of the intestinal tract to assimilate dietary fat and protein (nitrogen) following total removal of the stomach. Although the surgical literature abounds with clinical impressions of nutritional status following total gastrectomy, there are relatively few reports of metabolic studies performed in patients and animals. A critical analysis of these published metabolic studies will be reported separately in an article reviewing the literature with respect to nutrition following total gastrectomy. It need only be mentioned here that the reported metabolic studies are few in number, are conflicting in their results, are in some instances clouded by lack of adequate controls, and in other instances are complicated by the factor of recurrent cancer.

Accordingly, there is need for a definitive evaluation of fat and protein assimilation following total gastrectomy. In an effort to accomplish this purpose, metabolic studies have been performed on a series of dogs which had been submitted to total gastrectomy. By utilizing experimental animals as the subjects of these studies it is possible to evaluate the nutritional status following total removal of the stomach without the complicating factor of recurrent or residual carcinoma.

METHOD OF STUDY

A total of thirty-nine individual seven-day metabolic periods were studied in a series of 13 dogs which had been subjected to total gastrectomy. The studies were performed at times varying from 2 to 9 months after operation. Successive metabolic periods studied in the same animal were not necessarily consecutive but in most instances a varying interval of time elapsed between successive metabolic periods. The animals were given constant daily diets calculated and chemically analyzed to furnish 80 calories per kilogram of body weight and containing 4 Gm. of fat and 5 Gm. of protein per kilogram of body weight. Any food not eaten was weighed and subtracted from the total intake. Fecal collection periods were demarcated with carmine markers. The feces for each period were weighed, homogenized in a Waring blender, and fat and total nitrogen determined on aliquot samples. Nitrogen was determined using Hoffman's photelometric modification of the Koch and McMeekin direct

Received for publication, Aug. 13, 1951.

Nesslerization Kjeldahl micro-method.[2] Fecal fat was determined using the Soxlet method. Similar metabolism periods were performed on 6 normal dogs for controls.

RESULTS

Nitrogen Assimilation.—The data obtained in the study of nitrogen assimilation in dogs submitted to total gastrectomy, as compared with normal dogs,

TABLE I. METABOLISM STUDIES OF NITROGEN ASSIMILATION

DOG	7-DAY METABOLIC PERIOD	NITROGEN IN DIET (GM./7 DAYS)	% DIET TAKEN	ACTUAL NITROGEN INTAKE (GM./7 DAYS)	NITROGEN EXCRETED IN FECES (GM./7 DAYS)	% INGESTED NITROGEN IN FECES
Dogs With Total Gastrectomy						
1	1	43.1	100	43.1	19.6	45.4
	2		100	43.1	29.2	67.5
2	3	42.0	97.5	41.0	15.9	38.6
	4		100	42.0	23.9	56.8
3	5	78.4	100	78.4	27.8	35.5
	6		78.5	61.5	32.9	53.5
4	7	70.0	100	70.0	31.7	45.3
	8		85.7	60.0	19.7	32.8
5	9	65.0	72.5	47.1	28.5	60.5
	10		100	65.0	44.9	69.0
6	11	59.4	100	59.4	22.6	38.0
	12		100	59.4	27.9	47.0
7	13	61.6	73.6	45.5	10.5	23.0
	14		100	61.6	29.1	47.2
	15		75.4	46.5	21.0	45.0
8	16	70.0	100	70.0	10.4	14.9
	17		100	70.0	20.2	28.8
	18		100	70.0	21.3	30.4
9	19	49.8	100	49.8	29.4	59.0
	20		100	49.8	25.5	51.3
	21		100	49.8	24.0	48.3
10	22	66.0	94.0	62.0	17.1	27.6
	23		78.0	51.5	11.5	22.4
	24		94.5	62.5	10.6	17.0
	25		100	66.0	24.9	37.8
	26		100	66.0	42.9	65.0
	27		76.4	50.5	22.9	45.4
	28		67.2	44.2	32.8	74.2
11	29	70.0	100	70.0	22.0	31.4
	30		92	64.5	11.9	18.5
	31		100	70.0	15.9	22.7
	32		100	70.0	16.8	24.0
	33		100	70.0	25.6	36.6
12	34	56.0	100	56.0	32.0	57.2
	35		80	44.8	43.0	96.0
13	36	87.0	100	87.0	19.5	22.4
	37		62.3	54.1	16.0	29.6
	38		94	81.8	22.2	27.2
	39		75.5	65.6	15.9	24.2
Average			92.4			41.5
Controls (Normal Dogs)						
1	1	72.3	100	72.3	8.1	11.2
2	2	70.0	100	70.0	5.0	7.2
3	3	74.0	100	74.0	13.8	18.6
4	4	70.0	100	70.0	9.8	14.0
5	5	66.0	100	66.0	9.8	14.8
6	6	70.0	100	70.0	7.8	11.2
Average			100			12.8

are presented in Table I. In the series of animals with total gastrectomy there was an average of 41.5 per cent of the ingested nitrogen excreted in the feces as compared with an average fecal nitrogen excretion of 12.8 per cent in normal animals. This difference is statistically of very high significance.[5] Graphic representation of the percentage of ingested nitrogen excreted in the feces during each seven-day metabolic period following total gastrectomy is presented in Fig. 1. It can readily be seen that for all periods the percentage fecal nitrogen excretion is greater than the average percentage excretion for normal dogs. The range was from 14.9 per cent to 96 per cent.

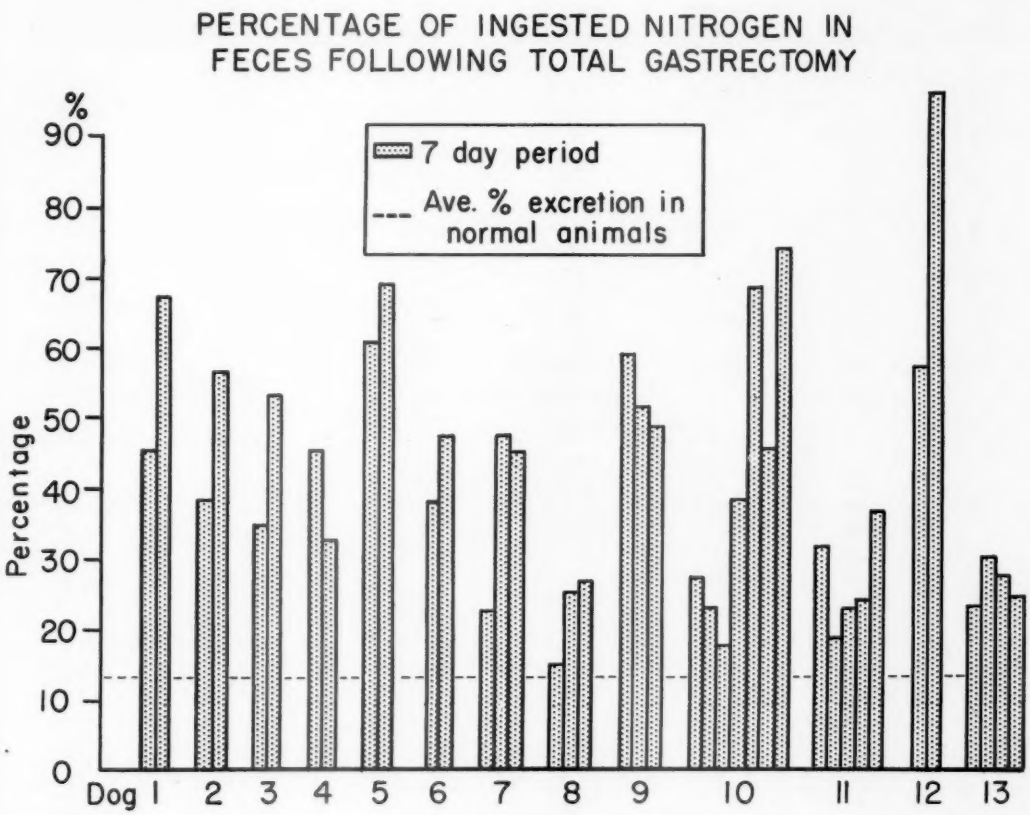


Fig. 1.

Fat Assimilation.—The data obtained in the study of fat assimilation in dogs submitted to total gastrectomy, as compared with normal dogs, are presented in Table II. In the dogs with total gastrectomy there was an average of 27.6 per cent of the ingested fat excreted in the feces as compared with an average fat excretion of 2.8 per cent in normal animals. Thus there was almost a tenfold increase in the average percentage fecal fat excretion in the animals with total gastrectomy. Again, this difference is statistically of very high significance.[5] Graphic representation of the percentage of ingested fat excreted in the feces during each individual seven-day metabolic period is presented in Fig. 2. It can readily be seen that the fecal fat excretion was in

all instances markedly greater in the animals with total gastrectomy than the average percentage fecal excretion in normal animals. The range was from 12.7 per cent to 66 per cent. Accordingly, it appears that a definite impairment in the assimilation of both protein and fat exists after total gastrectomy. However, impairment of fat assimilation appears to be several times greater than impairment of protein assimilation.

TABLE II. METABOLISM STUDIES OF FAT ASSIMILATION

DOG	7-DAY METABOLIC PERIOD	FAT IN DIET (GM./7 DAYS)	% DIET TAKEN	ACTUAL FAT INTAKE (GM./7 DAYS)	FAT EXCRETED IN FECES (GM./7 DAYS)	% INGESTED FAT IN FECES
			Dogs With Total Gastrectomy			
1	1	215.6	100.0	215.6	89.1	41.4
	2		100.0	215.6	72.5	33.6
2	3	210.0	97.5	205.2	66.8	32.6
	4		100.0	210.0	69.2	33.0
3	5	392.0	100.0	392.0	117.5	30.0
	6		78.5	308.0	112.0	36.4
4	7	350.0	100.0	350.0	71.3	20.4
	8		85.7	300.0	59.9	19.9
5	9	324.8	72.5	236.0	121.0	51.1
	10		100.0	324.8	83.0	28.2
6	11	297.0	100.0	297.0	86.0	28.9
	12		100.0	297.0	86.0	28.9
7	13	308.0	73.6	217.0	30.7	14.3
	14		100.0	308.0	67.8	22.0
	15		75.4	232.1	37.2	16.0
8	16	350.0	100.0	350.0	44.6	12.7
	17		100.0	350.0	101.7	29.0
	18		100.0	350.0	115.5	33.0
9	19	249.0	100.0	249.0	34.1	13.7
	20		100.0	249.0	122.0	49.0
	21		100.0	249.0	65.7	26.4
10	22	330.0	94.0	310.0	38.8	12.5
	23		78.0	257.0	54.5	21.2
	24		94.5	312.0	48.1	15.4
	25		100.0	330.0	66.4	20.1
	26		100.0	330.0	109.0	33.0
	27		76.4	252.0	106.0	42.0
	28		67.2	222.0	59.3	26.7
11	29	350.0	100.0	350.0	49.6	14.2
	30		92.0	322.0	58.3	18.1
	31		100.0	350.0	60.5	17.3
	32		100.0	350.0	40.5	11.6
	33		100.0	350.0	63.6	18.2
12	34	280.0	100.0	280.0	101.0	36.0
	35		80.0	224.0	148.0	66.0
13	36	435.0	100.0	435.0	139.1	32.0
	37		62.3	271.0	92.7	34.2
	38		94.0	409.0	94.0	23.0
	39		75.5	328.0	105.8	32.2
Average			92.4			27.6
			Controls (Normal Dogs)			
1	1	361.0	100.0	361.0	5.9	2.5
2	2	350.0	100.0	350.0	12.3	3.5
3	3	370.0	100.0	370.0	13.7	3.7
4	4	350.0	100.0	350.0	6.3	1.8
5	5	330.0	100.0	330.0	10.3	3.1
6	6	350.0	100.0	350.0	8.1	2.3
Average			100.0			2.8

DISCUSSION

Several factors of fat and protein digestion and absorption are effected by total removal of the stomach. These factors may be responsible in varying degrees for the impairment of fat and protein assimilation demonstrated following total gastrectomy.

1. *Loss of the Digestive Function of the Stomach.*—It does not seem probable that the absence of either the digestive action of pepsin or the weak digestive action of gastric lipase could be responsible for the marked nutritional disturbances which occur following total gastrectomy. The excellent nutritional status noted in many patients suffering from pernicious anemia (where pepsin is either absent or inactive because of concomitant achlorhydria) is strong evidence against loss of pepsin as a major causative factor of the nutritional derangement which occurs following total gastrectomy.

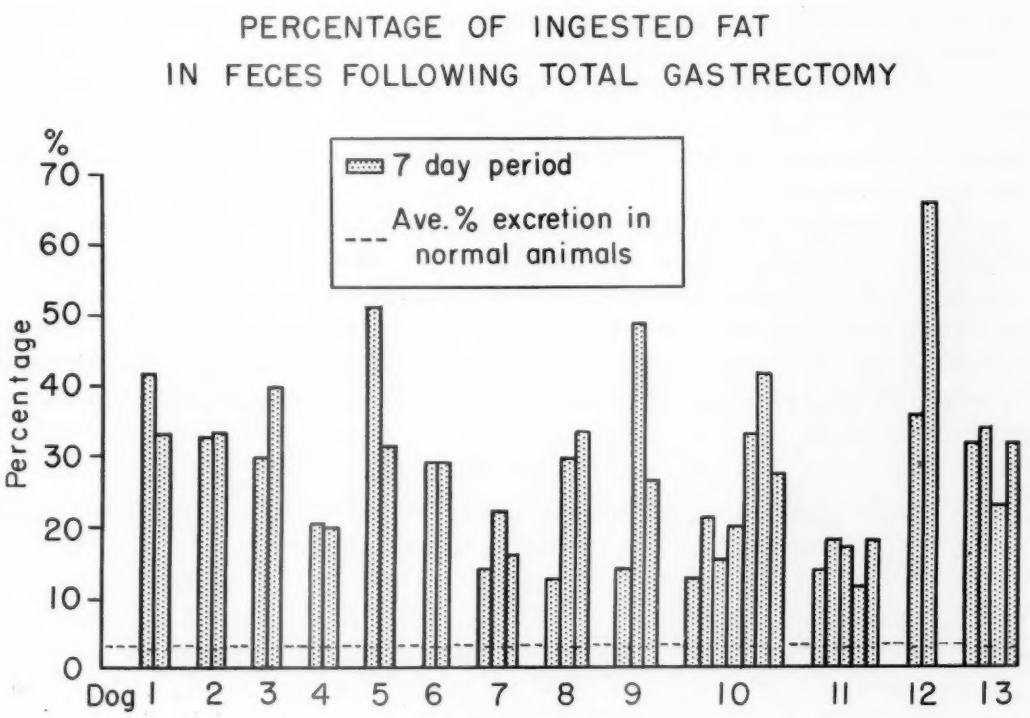


Fig. 2.

2. *Loss of the Triturating Function of the Stomach.*—It appears unlikely that loss of the triturating, or mixing, function of the stomach plays a major role in the nutritional impairment which occurs after total gastrectomy. In the metabolic studies reported in this paper the food was finely ground, and no grossly unchanged food was noted in the feces of these animals after total gastrectomy.

3. *Decreased Stimulation of Pancreatic Secretion.*—With the removal of the stomach the secretagogic effect of hydrochloric acid upon the pancreas is lost. Furthermore, in the operation of total gastrectomy, a vagotomy is performed.

Vagotomy, as has been shown by Shingleton and co-workers[4] results in a decreased secretion of pancreatic juice to various stimuli. Moreover, when an esophagojejunostomy type of anastomosis is performed, the secretagogic effect of food itself might be expected to be decreased. That the loss of the secretagogic effect of hydrochloric acid may not be an important factor is again suggested by the lack of serious nutritional impairment in many patients with achlorhydria.

4. *Improper or Inadequate Mixing of Food With Pancreatic and Biliary Secretions.*—In the normal individual there is a physiologic increase in secretion of bile and pancreatic juice following ingestion of food. Following total gastrectomy it is conceivable that the ingested food might be well down the intestinal tract before the increased amounts of pancreatic and biliary secretion are delivered into the upper intestine. Furthermore, when an esophagojejunostomy type of anastomosis is performed after total gastrectomy, the pancreatic and biliary secretions would have to traverse the entire duodenum and afferent jejunal limb before making contact with the food; and thus significant quantities of these juices might be reabsorbed before reaching the food.

5. *Increased Intestinal Motility.*—It has been shown by Ivy[3] and also by Emery[1] that in dogs the passage of food down the intestinal tract is more rapid following total gastrectomy. Thus there would be less time for intestinal digestion and absorption.

6. *Loss of the Reservoir Function of the Stomach.*—The stomach serves as a reservoir and releases food into the intestine intermittently and in small amounts. The loss of this function may be a factor of major importance in the nutritional impairment which occurs after total gastrectomy. Emery[1] noted in a study of one totally gastrectomized dog that fat and nitrogen assimilation returned to normal when the animal was fed in small amounts at frequent intervals.

SUMMARY

1. Thirty-nine individual seven-day metabolism periods were studied in a series of 13 dogs which had been subjected to total gastrectomy.

2. There was impairment of both fat and protein assimilation following total gastrectomy. An average of 41.5 per cent of the ingested nitrogen was excreted in the feces of the dogs with total gastrectomy as compared with an average fecal nitrogen excretion of 12.8 per cent in normal animals. Likewise an average of 27.6 per cent of the ingested fat was excreted in the feces of the animals with total gastrectomy as compared with an average fecal excretion of 2.8 per cent in normal animals.

REFERENCES

1. Emery, E. S., Jr.: The Cause of Faulty Digestion in Dogs Without Stomachs, Am. J. Digest. Dis. & Nutrition 2: 599-608, 1935.
2. Hoffman, W. S.: Photelometric Clinical Chemistry, New York, 1941, William Morrow & Company.
3. Ivy, A. C.: The Effects of Gastrectomy in Animals, Am. J. Digest. Dis. 7: 500-502, 1940.
4. Shingleton, W. W., Fawcett, B., and Vetter, J. S.: Pancreatic Secretion and Response to Secretion After Vagotomy and Sympathectomy, Surgical Forum American College of Surgeons, Philadelphia, 1951, W. B. Saunders Company.
5. Snedecor, A. W.: Statistical Methods, Ames, 1946, Iowa State College Press.

THE EFFECTS OF PARTIAL GASTRECTOMY ON CANINE EXTERNAL PANCREATIC SECRETION

DAVID ANNIS, M.B., F.R.C.S.,* AND GEORGE A. HALLENBECK, M.D.,**
ROCHESTER, MINN.

CONTROL of the secretion of pancreatic juice is intimately related to the activity of the stomach. Although a psychic phase of external pancreatic secretion, mediated through the vagus nerves, can be demonstrated in the dog, the greater part of the secretory response of the pancreas to a meal results from the entry of the products of gastric digestion into the upper part of the small intestine. Partial gastric resection inevitably alters the functioning of the stomach. Therefore, it seemed possible that removal of a large part of the stomach might influence the secretory response of the pancreas to a meal. The experiments on which this report is based were carried out to study this problem.

METHODS

In 5 dogs the pancreatic secretory responses to the ingestion of a meal of meat were obtained before and after partial gastrectomy. To detect any possible change in the capacity of the pancreas to secrete in response to standardized stimuli independent of gastric activity, the response of the pancreas to the intravenous injection of secretin and to the intraduodenal instillation of a one-tenth normal solution of hydrochloric acid also was observed before and after gastrectomy.

Pancreatic juice was collected by the method described by Thomas and Crider[1] and modified by Scott and his co-workers.[2] Briefly, this method takes advantage of the fact that the common bile duct and the major pancreatic duct enter the duodenum separately so that the pancreatic duct can be cannulated independently. Under aseptic surgical conditions the minor pancreatic duct was tied and divided. One end of the spool-shaped Thomas cannula was inserted into the lumen of the duodenum opposite the entrance of the major pancreatic duct, and the other was brought out through a stab incision in the abdominal wall. During experiments, access into the duodenum was obtained by opening the Thomas cannula. Through this a fine olive-tipped glass tube was introduced into the papilla of the major pancreatic duct in much the same manner as a ureter is catheterized transvesically. To prevent the loss of gastrointestinal contents other than pancreatic juice, the opening in the Thomas cannula was closed around the glass tube by a rubber diaphragm made from a finger cot. Throughout the experiments care was taken to insure a free flow of juice from the cannula.

Between experiments the glass tube was removed and the duodenal cannula was kept closed. Pancreatic juice then entered the duodenum normally.

Received for publication, Aug. 10, 1951.
*Fellow in Experimental Surgery, Mayo Foundation, University of Minnesota.
**Division of Surgery, Mayo Clinic.

As a result dogs could be maintained indefinitely in a good state of nutrition since there was no continuous loss of pancreatic enzymes, fluid or electrolytes.

Food was withheld from each dog for twenty to thirty-six hours before an experiment was begun. After the pancreatic duct had been cannulated, juice was collected from the dog for fifteen minutes.

When the stimulus for secretion was a meal, 200 Gm. of cooked horse meat were fed and the resultant pancreatic juice was collected at intervals of fifteen minutes for three hours. After gastrectomy it appeared desirable that the study should extend over a longer period. Accordingly, additional data were collected for the period from the fourth to the ninth hour, inclusive, after feeding. This extended study was limited to 1 or 2 experiments on each dog.

When the stimulus for secretion was secretin, 15 units of secretin* were injected intravenously. This procedure was repeated at least twice, the juice secreted after the first injection being discarded because it might contain residual juice present in the ducts during fasting. In other experiments 30 c.c. of a one-tenth normal solution of hydrochloric acid were placed into the duodenum as the stimulus for secretion. In both of these groups of experiments juice secreted during twenty minutes following application of the stimulus was taken for analysis.

The volume of the juice was recorded. The bicarbonate content of the juice was estimated by a method of Van Slyke[3] and recorded as milliequivalents. The tryptic activity was estimated by the method of Anson and Mirsky[4] and recorded in units of milligrams of tyrosine liberated from a hemoglobin substrate per milliliter of pancreatic juice. The nitrogen content of the juice was determined by the Kjeldahl micro-method.

The partial gastrectomies were carried out by removing approximately three-fourths of the stomach, including all of the pyloric antrum. In 2 dogs, an end-to-end gastroduodenostomy of the Billroth I type was performed. In 3 dogs, the duodenal stumps were closed and the operation completed by using a Polya type of gastrojejunal anastomosis. The ligament of Treitz was divided, and the afferent limb of jejunum was made only long enough to insure gastrojejunal anastomosis without tension.

After gastrectomy, experiments were postponed until the animals were eating well and could tolerate the meal of meat without regurgitation. In most animals this occurred within four weeks after the operation. Postoperative experimental observations were made periodically over a period varying from one to fifteen months.

Information on the rate of emptying of the gastric remnant was obtained from serial roentgenograms made after feeding of the standard meal rendered radiopaque by the addition of barium sulfate.

RESULTS

In 4 of the 5 dogs the volume, total bicarbonate, total nitrogen, and trypsin activity of pancreatic juice secreted during the first three hours after feeding

*We are indebted to Eli Lilly & Company, Indianapolis, Ind., for the secretin used in this study.

were greatly reduced after partial gastrectomy. In the fifth dog, a transient reduction immediately after gastrectomy was followed by resumption of essentially normal pancreatic secretion later. Data collected on juice secreted from the fourth to ninth hours, inclusive, after feeding showed that in some animals the secretion increased at some time during this period.

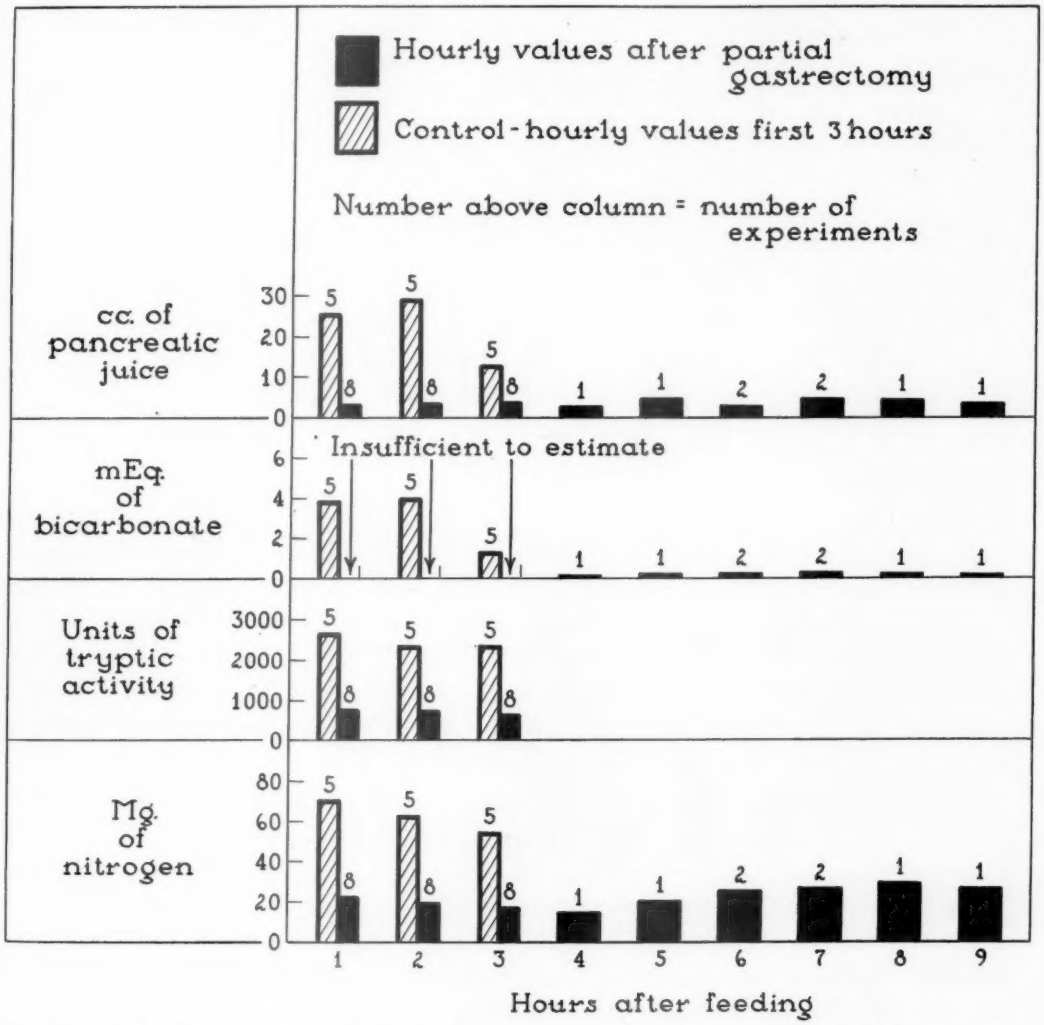

Hourly values after partial gastrectomy
Control - hourly values first 3 hours
Number above column = number of experiments
cc. of pancreatic juice
mEq. of bicarbonate
Insufficient to estimate
Units of tryptic activity
Mg. of nitrogen
Hours after feeding

Fig. 1.—Effect of Billroth I partial gastrectomy on the secretory response of the pancreas to a meal of meat (dog No. 1).

In dog No. 1, the mean volume, tryptic activity, and total nitrogen during the first 3 hours after feeding following a Billroth I type of gastrectomy were reduced by 84.7, 71.2 and 68.5 per cent, respectively, compared with preoperative control values (Table I). These reductions were maintained from the fourth to the ninth hours, inclusive, after feeding (Fig. 1). This response was unchanged over a period of 15 months after gastrectomy.

In dog No. 2, which also underwent a Billroth I type of gastrectomy, similar reductions in the variables measured occurred during the first 3 hours after

feeding (Table I). However, beginning in the fifth hour after feeding and increasing through the seventh hour, there occurred an acceleration of the flow of pancreatic juice, and an increase in the output of bicarbonate, trypsin, and nitrogen (Fig. 2). Observations on this dog extended over a period of 8 months after gastrectomy.

TABLE I. EFFECT OF PARTIAL GASTRECTOMY ON THE SECRETORY RESPONSE OF THE CANINE PANCREAS TO A MEAL OF MEAT

DOG	PER CENT CHANGE IN THE FIRST 3 HOURS OF PANCREATIC SECRETORY RESPONSE TO A MEAL AFTER PARTIAL GASTRECTOMY			
	VOLUME	BICARBONATE	TRYPSIN ACTIVITY	NITROGEN
1	−84.7	Juice insufficient for estimation	−71.2	−68.5
2	−91.3	−91.8	−63.0	−79.0
3	−72.5	−84.4	−52.2	−64.7
4	−90.8	−93.6	−63.5	−73.9
5 Primary gastrectomy				
Early	−91.5	−92.9	−86.8	−89.3
Later	−6.5	+36.1	+27.2	−14.1
Secondary gastrectomy				
Early	−81.3	−83.0		−73.0
Later	+11.2	+51.6		−22.5

Dogs No. 3 and 4, each of which underwent a gastric resection with anastomosis of the Polya type, again showed the marked depression of pancreatic secretion during the first three hours after feeding (Table I). Each had an interval of more active secretion occurring later (Figs. 3 and 4). Observations on dog No. 3 extended over a period of 6 months; those on dog No. 4, over a period of only 1 month after operation. Therefore, no statement regarding the permanency of these changes can be made in the case of this last dog.

Dog No. 5 underwent a partial gastrectomy of the Polya type that differed from that performed on the others only in that approximately half, rather than three-fourths, of the stomach was removed. Like the others, this dog showed a reduction in pancreatic secretion 2 weeks after the operation. Between the third and fourth weeks after gastrectomy, the pancreatic secretory response to a meal was observed to have returned to a state which approached the normal. Three months after the initial gastrectomy, a second operation was performed and an additional 50 Gm. of stomach were removed, making a total of at least three-fourths of the organ which had been removed. Again, a low rate of postprandial pancreatic secretion was observed at 7 and 8 weeks after the secondary gastric resection, and again the animal recovered its ability to secrete nearly normal amounts of pancreatic juice in response to a meal at a later date (Table I, Fig. 5).

Comparison of the volume and nitrogen content of pancreatic juice secreted by these 5 dogs in response to secretin injected intravenously and to the one-tenth normal solution of hydrochloric acid placed in the duodenum before and after gastrectomy clearly indicates that although the responses are variable

the pancreas retains its ability to respond to these stimuli after the operation (Table II). We interpret this to mean that the reduction in the secretory response to a meal after partial gastrectomy was not due to an inability of the pancreas to respond to an adequate stimulus.

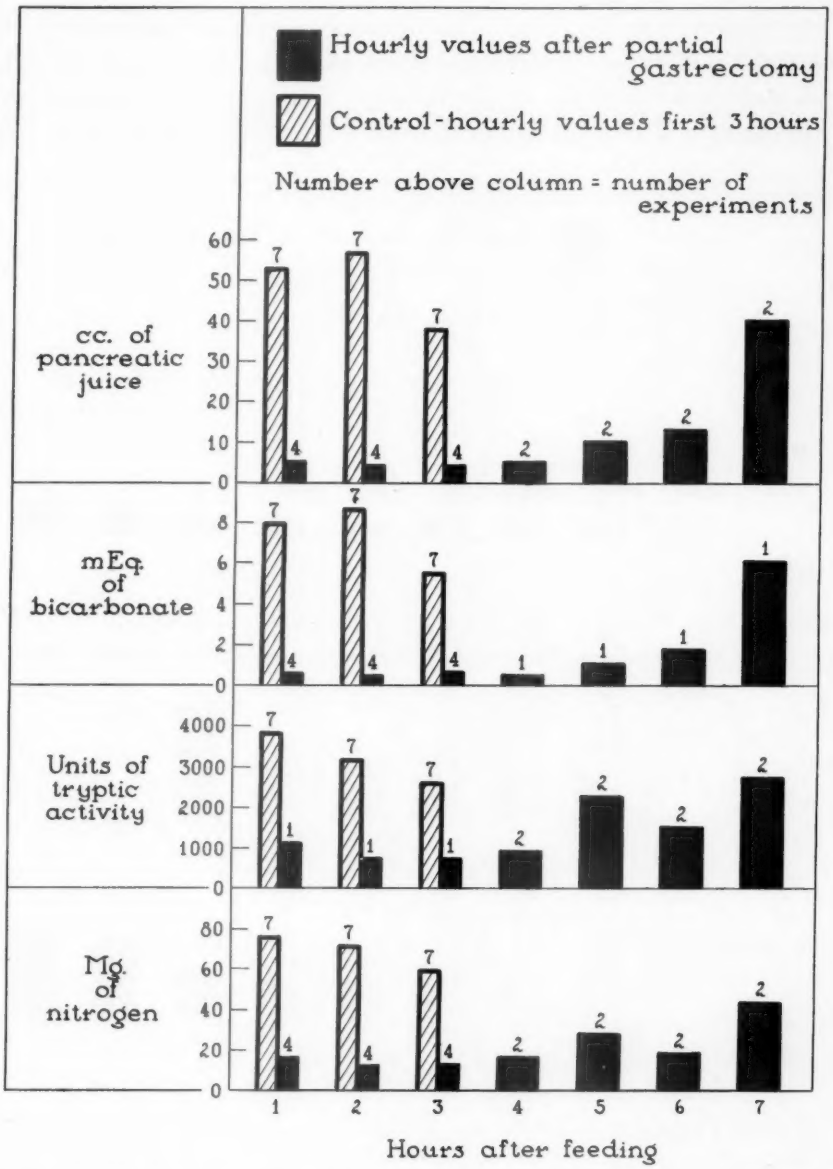

Hourly values after partial gastrectomy
Control-hourly values first 3 hours
Number above column = number of experiments
cc. of pancreatic juice
mEq. of bicarbonate
Units of tryptic activity
Mg. of nitrogen
Hours after feeding

Fig. 2.—Effect of Billroth I partial gastrectomy on the secretory response of the pancreas to a meal of meat (dog No. 2).

The question arose whether the increase in the rate of secretion that occurred during the fourth to the ninth hours after feeding in most of the dogs might be associated with a delayed emptying of the gastric remnant. To study this possibility, the dogs were fed a meal of meat similar to that used in the preceding experiments but rendered radiopaque by the addition of 30 Gm. of

barium sulfate. Serial roentgenograms were made during the digestion of this meal. Dogs No. 1, 2, 3, and 5 were available for this purpose. The percentage of the meal that remained in the gastric remnant was estimated at intervals after feeding. In a normal dog of similar size, approximately 50 per cent of this meal remained in the stomach at the end of the third hour and the stomach was empty after the sixth hour. The pattern of gastric emptying in dogs No. 1, 3, and 5 did not differ significantly from normal. Dog No. 2, however, had a delay in gastric emptying. Approximately 5 hours were required for 50 per cent of the meal to leave the stomach, and at the end of 9 hours an estimated

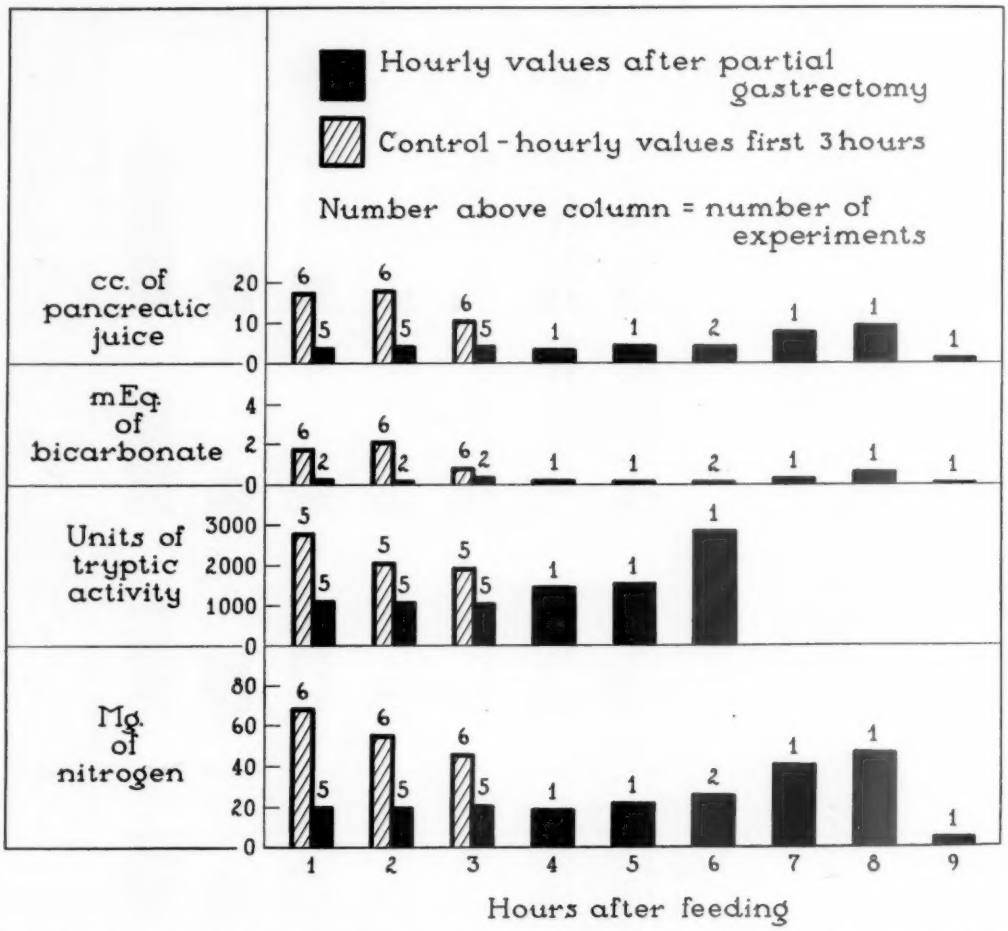

Hourly values after partial gastrectomy
Control - hourly values first 3 hours
Number above column = number of experiments
cc. of pancreatic juice
mEq. of bicarbonate
Units of tryptic activity
Mg. of nitrogen
Hours after feeding

Fig. 3.—Effect of Polya type of partial gastrectomy on the secretory response of the pancreas to a meal of meat (dog No. 3).

30 per cent of the meal still remained in the gastric remnant. This confirmed a clinical impression that this dog had delayed emptying of the remnant of the stomach, an impression based on the fact that there was a delayed appearance of ingested food in the duodenum as seen through the Thomas cannula. Furthermore, this food, when reaching the duodenum, appeared to be better digested than was the case in the other dogs. It may be significant that the late appearance of this partly digested food in the duodenum in dog No. 2 coincided with the late appearance of large quantities of pancreatic juice (Fig. 2).

COMMENT

The observation that canine postprandial pancreatic secretion was depressed after partial gastrectomy in 3 of the dogs for 6 to 8 months during which observations were made and depressed in a fifth dog for the 1 month during which observations could be made is not surprising in view of the close

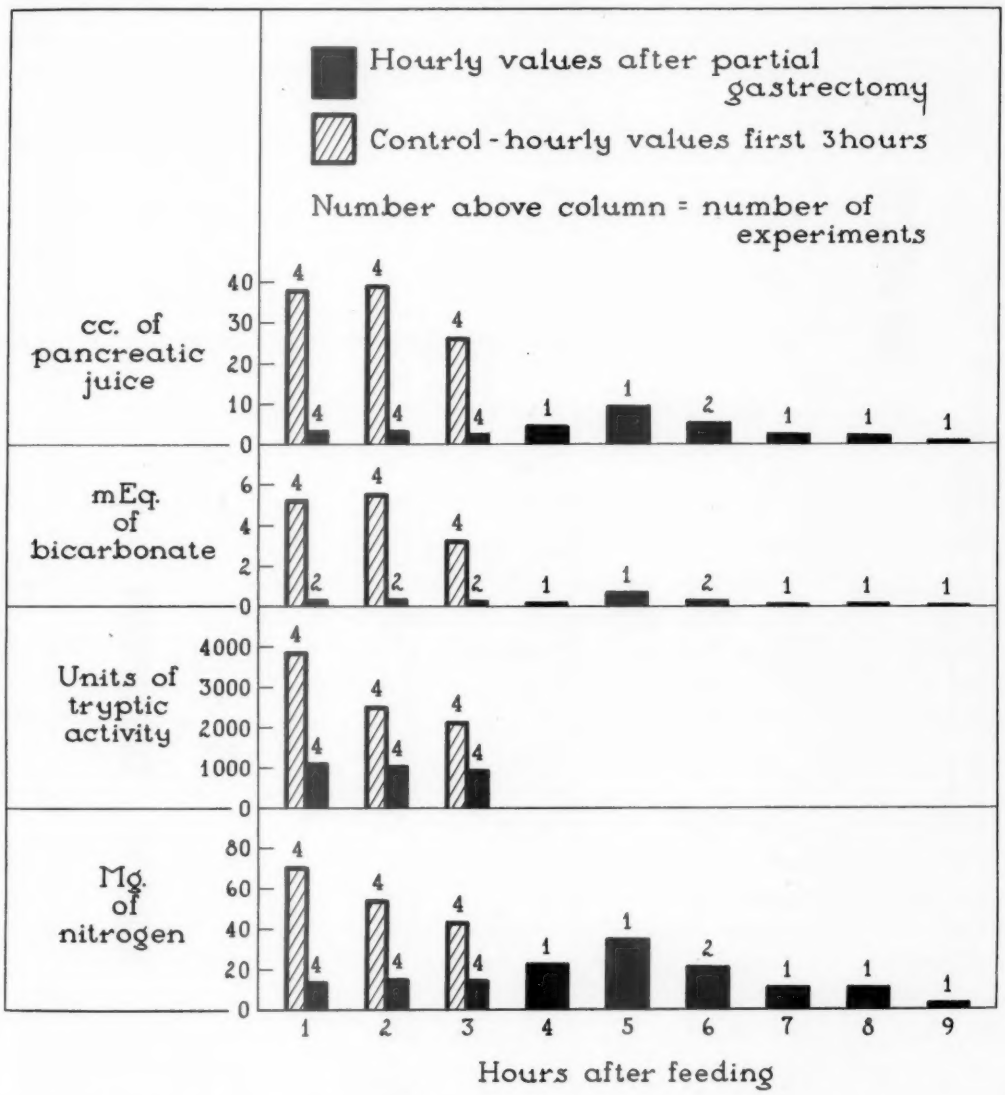

Hourly values after partial gastrectomy
Control - hourly values first 3 hours
Number above column = number of experiments
cc. of pancreatic juice
mEq. of bicarbonate
Units of tryptic activity
Mg. of nitrogen
Hours after feeding

Fig. 4.—Effect of Polya type of partial gastrectomy on the secretory response of the pancreas to a meal of meat (dog No. 4).

relationship between the digestive activity of the stomach and the normal stimulation of external pancreatic secretion. With this in mind, Richman and Colp[5] have proposed partial gastric resection plus vagotomy as treatment for chronic relapsing pancreatitis in the hope that pancreatic secretion might be diminished and that this in turn might prove beneficial. In the intact animal,

ingestion of a meal evokes a flow of acid gastric juice which, when mixed with food, forms a semifluid material, acid in reaction, designated chyme. Much of the protein is digested to soluble proteoses and peptones. The passage of this acid chyme into the duodenum results in the prompt secretion of pancreatic juice. Several mechanisms may be involved. The presence of acid in the intestine has long been known to stimulate the flow of pancreatic juice. The discovery by Bayliss and Starling[6] that acid in the intestine causes liberation

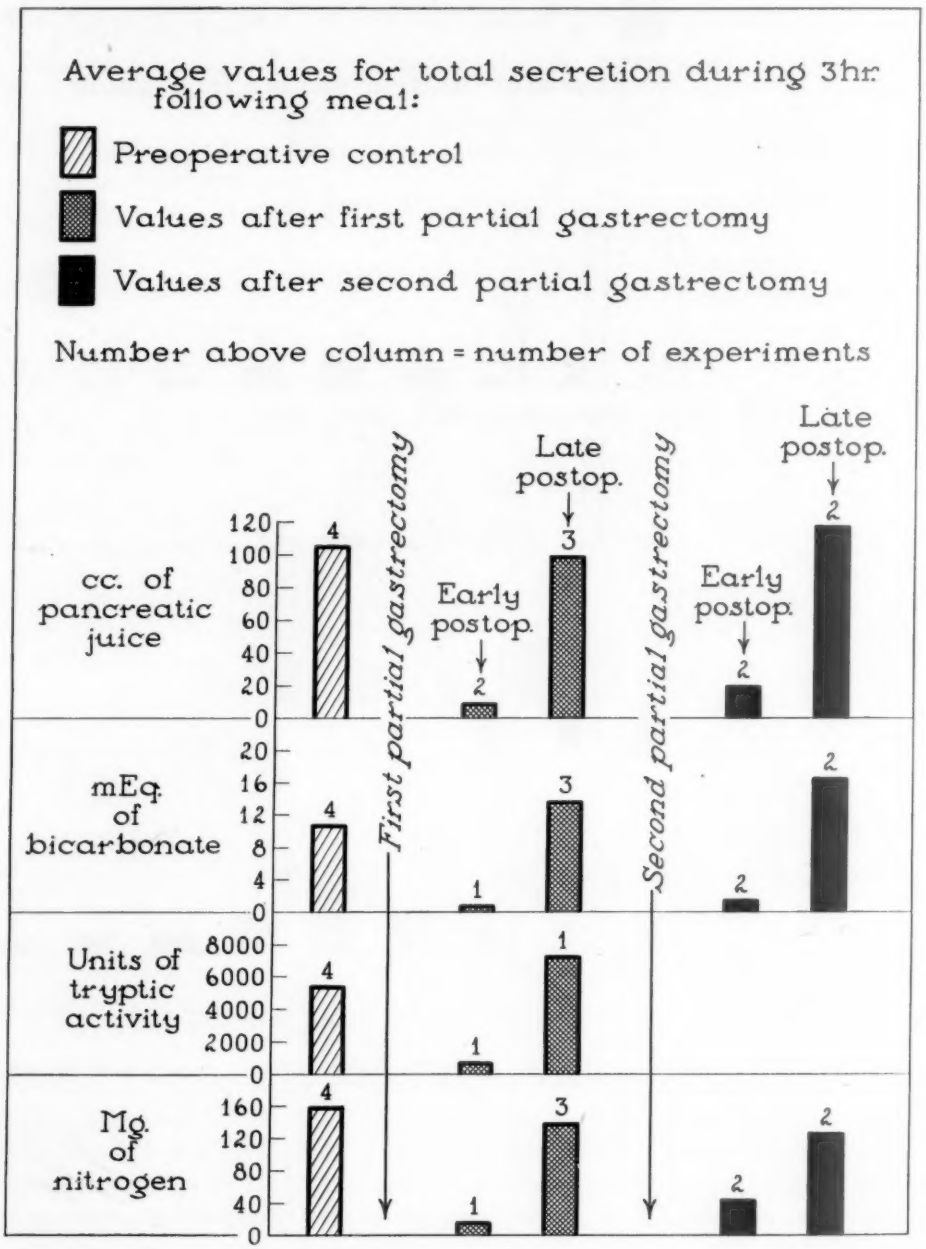


Fig. 5.—Effect of a Polya type of partial gastrectomy and of a secondary gastrectomy on the secretory response of the pancreas to a meal of meat (dog No. 5).

from the intestinal mucosa of a hormone, secretin, which stimulates pancreatic secretion via the blood stream, elucidated this mechanism. Recent evidence, summarized by Thomas,[7] indicates that this acid-secretin mechanism does not play a dominant role in the stimulation of canine pancreatic secretion during normal digestion. Peptones, proteoses, and some of the products of digestion of fat, when present in the intestine, are pancreatic secretagogues. Unlike acid, they result in a secretion rich in nitrogenous materials. This mechanism may be explained by liberation of pancreozymin,[8, 9] a more recently discovered hormone which is derived from the intestinal mucosa and stimulates the pancreas to secrete a juice rich in enzymes. Pancreatic secretion may also be stimulated by impulses carried over the vagus nerves.[10]

TABLE II. COMPARISON OF CANINE PANCREATIC SECRETORY RESPONSE TO SECRETIN AND TO HYDROCHLORIC ACID BEFORE AND AFTER PARTIAL GASTRECTOMY

	PER CENT CHANGE AFTER GASTRECTOMY WHEN STIMULUS WAS			
	SECRETIN		HYDROCHLORIC ACID	
DOG	VOLUME	NITROGEN CONTENT	VOLUME	NITROGEN CONTENT
1	+32.4	+16.1	+16.1	+28.7
2	−16.5	−77.1	+30.8	−19.1
3	+27.9	+124.6	−47.0	−52.0
4	+20.8	−13.1	+14.1	+22.0
5	+152.5	+83.2		

After gastric resection several changes may be expected, all of which could act to decrease the potency of the chyme as a pancreatic secretagogue.

A decrease in total hydrochloric acid secreted by the remaining stomach should permit its more complete neutralization by food prior to its entry into the small intestine. Since stimulation of canine pancreatic secretion by acid is not of major importance during normal digestion, diminution of acid alone cannot be held to account for all of the reduction in prandial pancreatic secretion observed after partial gastrectomy in this study.

Peptic digestion may be expected to be less complete in the resected than in the intact stomach, and the quantity of peptones and proteoses in the chyme should be diminished. Indeed, observations made through the Thomas cannulas in these dogs revealed the presence of obviously undigested particles of meat in greater quantities than were seen in intact animals. It is reasonable to assume that this factor was particularly important in producing the reduction in the secretion of pancreatic juice after feeding which was observed after partial gastrectomy.

It is possible that some of the vagus nerve supply to the pancreas could have been divided during the performance of partial gastrectomy, although we attempted to confine the dissection to tissues immediately adjoining the stomach. Because many of the fibers of the vagus nerves destined to reach the pancreas leave the region of the stomach near the esophagogastric junction and pass posteriorly through the celiac ganglion to the gland, we feel that partial gastric resection could not be expected to result in complete vagal denervation of the pancreas.

The method used in our experiments, in common with that used in most other reported studies of external pancreatic secretion, introduced an important deviation from the normal process of digestion in that pancreatic juice was removed for analysis and thus denied entry into the duodenum. In another study of intact dogs,[11] we found that this process alone results in secretion of a greater volume of pancreatic juice after feeding than is formed when all juice is placed at intervals into the intestine. The output of nitrogen and the trypsin activity were little affected by these manipulations. The evidence favored the conclusion that the greater output of pancreatic juice in this abnormal situation was related to activity of the acid-secretin mechanism brought into play by absence of the alkaline pancreatic fluid from the intestine. This phenomenon depends for its operation on secretion of adequate amounts of hydrochloric acid by the stomach. Since production of acid is usually reduced after partial gastrectomy, withdrawal of pancreatic juice can be expected to cause a greater increase in the volume of juice secreted before gastrectomy than afterward. Part of the reduction which we observed in the volume of pancreatic juice secreted after operation is probably accounted for in this manner. That only a part of this reduction can be so explained is evidenced by observations on dogs No. 1 and 2 on which data were available on the performance of the pancreas in response to the meal before gastrectomy when the dogs' pancreatic juice was placed in the duodenum at intervals. When these data, instead of values obtained when all juice was removed, are used as preoperative control values, the percentage reductions in volume of secretion after gastrectomy are changed from –84.7 to –67.8, and from –91.3 to –82.4, respectively. Thus these considerations do not invalidate the general conclusions reached in the present study. They probably do account in part for the observation that the volume and bicarbonate concentration of the juice were reduced to a greater degree than the concentration of nitrogen and trypsin (Table I).

Despite the changes observed in pancreatic secretion, the dogs remained in a good state of nutrition after they had fully recovered from the operative procedures. It was noted that the animals were able to gain weight, had no diarrhea, and did not present an unusual amount of grossly visible undigested food in the feces. This is understandable in view of Dragstedt's[12] experience that removal of from 80 to 90 per cent of the pancreas causes no defect in the digestion and absorption of foodstuffs in the dog provided the remaining pancreas remains in connection with the intestine.

In human beings, failure to gain weight is a rather common occurrence after partial gastrectomy. Doubtless, many factors are involved. In some cases, insufficient caloric intake due to discomfort occasioned by eating or to anorexia may be an evident cause of loss of weight. In others, impairment of absorption of foodstuffs may play an important role. Increased fecal loss of fat and, to a lesser extent, of nitrogen have been demonstrated in intake-excretion studies on human beings after partial gastrectomy by Wollaeger and his associates.[13, 14] It is possible that diminished external pancreatic secretion after gastrectomy may be one of several factors contributing to this syndrome.

Perhaps the most frequent use of partial gastrectomy in clinical surgery is in the treatment of duodenal ulcer. The objective is to reduce the quantity of acid gastric juice entering the small intestine to quantities which can be adequately neutralized by duodenal contents. The reduction in the volume and bicarbonate concentration of pancreatic secretion observed after gastrectomy in this study might erroneously appear to counteract the benefit gained by the operation. However, the fact that the pancreas responds normally to acid placed in the intestine after gastrectomy indicates that the gland can secrete in response to such acid as may be secreted by the gastric remnant if called upon to do so. The protective secretin mechanism remains unimpaired.

CONCLUSIONS

1. In 4 of 5 dogs the volume, bicarbonate content, and nitrogen content of pancreatic juice secreted in response to a meal of meat were decisively reduced after resection of three-fourths of the stomach. In a fifth dog, a temporary reduction in postprandial pancreatic secretion after gastrectomy was followed by resumption of the normal secretory pattern.

2. The response of the canine pancreas to hydrochloric acid placed in the duodenum and to secretin injected intravenously was unchanged by partial gastrectomy.

REFERENCES

1. Thomas, J. E., and Crider, J. O.: A Quantitative Study of Acid in the Intestine as a Stimulant for the Pancreas, Am. J. Physiol. **131**: 349-356, 1940.
2. Scott, V. B., Collignon, U. J., Bugel, H. J., and Johnson, G. C.: The Relation of External Pancreatic Secretion to Variations in Blood Sugar, Am. J. Physiol. **134**: 208-218, 1941.
3. Van Slyke, D. D.: Studies of Acidosis. XVIII; Determination of the Bicarbonate Concentration of the Blood and Plasma, J. Biol. Chem. **52**: 495-499, 1922.
4. Anson, M. L., and Mirsky, A. E.: The Estimation of Trypsin With Hemoglobin, J. Gen. Physiol. **17**: 151-157, 1933.
5. Richman, Alexander, and Colp, Ralph: Chronic Relapsing Pancreatitis Treatment by Subtotal Gastrectomy and Vagotomy, Ann. Surg. **131**: 145-158, 1950.
6. Bayliss, W. M., and Starling, E. H.: The Mechanism of Pancreatic Secretion, J. Physiol. **28**: 325-353, 1902.
7. Thomas, J. E.: The External Secretion of the Pancreas, Springfield, Ill., 1950, Charles C Thomas, publisher, pp. 62-84.
8. Harper, A. A., and Raper, H. S.: Pancreozymin, a Stimulant of the Secretion of Pancreatic Enzymes in Extracts of the Small Intestine, J. Physiol. **102**: 115-125, 1943.
9. Wang, C. C., and Grossman, M. I.: Physiological Determination of Release of Secretin and Pancreozymin From Intestine of Dogs With Transplanted Pancreas, Am. J. Physiol. **164**: 527-545, 1951.
10. Pavlov, I. P.: The Work of the Digestive Glands, Trans. by W. H. Thompson, ed. 2, London, 1910, Charles Griffin & Company, Limited.
11. Annis, David, and Hallenbeck, G. A.: Effect of Excluding Pancreatic Juice From Duodenum on Secretory Response of Pancreas to a Meal, Proc. Soc. Exper. Biol. & Med. **77**: 383-385, 1951.
12. Dragstedt, L. R.: Some Physiologic Problems in Surgery of the Pancreas, Ann. Surg. **118**: 576-589, 1943.
13. Wollaeger, E. E., Comfort, M. W., Weir, J. F., and Osterberg, A. E.: The Total Solids, Fat and Nitrogen in the Feces: II. A Study of Persons Who Had Undergone Partial Gastrectomy With Anastomosis of the Entire Cut End of the Stomach and the Jejunum (Polya Anastomosis), Gastroenterology **6**: 93-104, 1946.
14. Wollaeger, E. E.: Disturbances of Gastrointestinal Function Following Partial Gastrectomy, Postgrad. Med. **8**: 251-259, 1950.

SUPPURATIVE PELVIC THROMBOPHLEBITIS

IV. Results

A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Vessels

Conrad G. Collins, M.D.,*§ Robert O. Norton, M.D.,* Edward W. Nelson, M.D.,* B. Bernard Weinstein, M.D.,* Jason H. Collins, M.D.,*§ and Herman D. Webster, Jr., B.S.,** New Orleans, La.

PREVIOUS publications[1-3] presented an analysis of 70 patients in whom ligation of the inferior vena cava and ovarian vessels was performed for suppurative pelvic thrombophlebitis, from the standpoint of incidence, pathology, etiology, symptomatology, diagnosis, and surgical technique. This communication presents the results in this series of cases as determined by frequent follow-up studies.

All patients in this series were operated upon between Feb. 2, 1942, when the first operation was performed, and January, 1950. Follow-up studies were conducted as late as July 1, 1951. Forty-two patients have been followed longer than two years (Table I). Six of the operations in this series were performed by members of the Department of Obstetrics and Gynecology of the Louisiana State University School of Medicine, the remainder by members of the Department of Obstetrics and Gynecology of Tulane University School of Medicine. With the exception of 2 patients, all were supervised preoperatively, at operation, and postoperatively by one or all of us. Most of the cases were under the direction of the senior author. Repeated follow-up observations have been conducted by us and detailed studies of the vascular status of the extremities have been made in many cases by Dr. Burch and associates in the Department of Medicine, Tulane University School of Medicine.

CASE MORTALITY RATE

It is to be emphasized that ligation was performed on patients only if they failed to respond to the medical therapy popularly employed at that time, or showed pulmonary infarction and had the worst type of pelvic infection one can encounter. Of these 70 seriously ill patients, 62 survived (eighty-nine per cent) and 8 died (eleven per cent). Thus, many lives were salvaged. All patients who died within one year of operation were considered operative failures, for it is our belief that ligation accomplishes nothing if the patient dies of distant septic metastasis even though the vena cava and ovarian vessels are

Aided by a grant from the Anonymous Research Fund.
Received for publication, Aug. 9, 1951.

*From the Department of Obstetrics and Gynecology, Tulane University of Louisiana, School of Medicine and The Tulane Unit, Charity Hospital of Louisiana.
**Predoctoral Fellow, National Foundation for Infantile Paralysis.
§From the Ochsner Clinic.

TABLE I. FOLLOW-UP IN YEARS OF 62 PATIENTS

YEARS FOLLOWED	CASES
0-1	12
1-2	8
2-3	11
3-4	11
4-5	6
5-6	5
6-7	1
7-8	3
8-9	4
9-10	1
Total	62

successfully ligated (Table II). In fact, 4 of the 8 patients who died were operated on from 9 to 21 days following admission to the hospital. Death did not result from the operation, but from delay in operating. It has been our experience that if chemotherapeutic and antibiotic agents are to produce results, great improvement will be noted within 4 to 5 days of institution of therapy. Some believe that ligation of the vena cava in critically ill patients results in a high mortality rate. This has not been our experience, as in our series, in only one patient (H. A., Table II) who died immediately after operation could the procedure have conceivably been responsible for death, although the pathologic changes noted at operation and autopsy make this questionable. It is the critically ill patient who most needs ligation.

TABLE II. CAUSES OF DEATH

PATIENT	ADMITTED	OPERATED UPON	DIED	CAUSE OF DEATH
H. A.	4/15/42	4/18/42	4/18/42	Peritonitis, pulmonary infarct, splenic infarct, postabortal pyometra, thrombus which involved superior vena cava and auricle of heart, postabortal (autopsy)
M. T.	1/ 4/45	1/25/45	1/30/45	Septicemia, postabortal (clinical)
A. B.	3/15/46	3/20/46	6/28/46	Ruptured mycotic aneurysm, inferior mesenteric artery, acute bacterial endocarditis superimposed on old rheumatic valvulitis, postabortal (autopsy)
E. F.	6/ 8/46	6/21/46	7/14/46	Subacute bacterial endocarditis, postabortal (clinical)
G. C.	12/16/47	12/18/47	12/23/47	Septicemia *(Staphylococcus aureus)*, postabortal (clinical)
F. S.	9/30/48	10/ 9/48	11/17/48	Possible lupus erythematosus, fibrinous pericarditis, granular vegetations of mitral valve, retained secundines, postabortal (autopsy)
M. A.	8/30/46	9/11/46	9/20/46	Uremia, pyelonephritis, pleural effusion, bronchopneumonia, pulmonary tuberculosis caseous right lobe, perirectal abscess, infarct of spleen (massive hemorrhage from abscess wall) (autopsy)
A. B.		8/ 1/49	9/ 8/49	Uremia, atelectasis, transfusion reaction (autopsy)

Four patients died of unrelated conditions, 2, 3, 2, and 7 years, respectively, after operation. As can be seen from Table III, death could in no way

be attributed to complications resulting from ligation of the vena cava and ovarian vessels. Until the time of death all had normal menstrual function, no evidence of varicosities, edema, or ulceration, and led normal active lives.

TABLE III. CAUSES OF LATE DEATHS

PATIENT	OPERATION	DEATH	CAUSE OF DEATH
O. D.	1942	1944	Arsenical encephalopathy
G. L.	1942	1945	Third degree burns of body
J. D.	1942	1944	Hemorrhage at time of lobectomy
M. N.	1942	1949	Unknown

RETURN VENOUS CIRCULATION

The venous channels involved in the flow of blood from the lower extremities and pelvis, following ligation of the inferior vena cava, have been repeatedly investigated.[4-6] Robinson,[7] in our laboratories, reported a study of the problem by injecting neoprene into stillborn infants after ligating the inferior vena cava and ovarian vessels, and presented an excellent review of the literature on this subject. All studies show that the vertebral, lumbar, azygos, and portal systems are the most important collateral routes, and that the hemorrhoidal plexus and superficial veins of the trunk are the least important. This observation has been substantiated by our infrared photographic studies of the abdomen and legs in patients who have had ligation of the vena cava and ovarian vessels.[8] Furthermore, varicostities of the abdominal wall, flank, thigh, or legs have not developed in any of our patients with the exception of one woman who has varicosities of the legs, which, however, existed prior to operation and were not made worse by ligation of the inferior vena cava and ovarian vessels.

In 8 cases, hysterectomy was performed for fibroid tumors or symptoms due to chronic salpingo-oophoritis, 2 months to 6 years following ligation of the inferior vena cava and ovarian vessels. At the time of laparotomy for these latter conditions a careful survey was made of the abdominal and pelvic vessels. No increase in capillary bleeding was encountered in the abdominal wall, nor were any dilated veins seen. The inferior epigastric vessels were found to be of normal caliber and there was no increase in size of the preperitoneal vessels. In two cases, dilated uterine veins were observed, but this is also found in some cases of chronic salpingo-oophoritis or fibroids. The retroperitoneal vessels were not engorged or dilated. This is further proof that the vertebral and lumbar veins are the main collaterals. In no instance was the liver enlarged or atrophic. Hemorrhoids have not developed in any case. In our opinion these two observations tend to lessen the importance of the hemorrhoidal plexus as a major collateral.

CONDITION OF LOWER EXTREMITIES

The immediate reaction of the lower extremities to ligation of the inferior vena cava is variable. In some cases no change whatsoever is noted (Fig. 1). In others mild edema appears within 2 to 10 days, persists for a few weeks and

gradually disappears entirely. In many cases moderate edema will develop and persist for a few weeks to a few months. In a few instances the edema may involve the entire leg and thigh. This is especially true if swelling was present prior to ligation (Fig. 2). In all cases, no matter how much edema is noted in the immediate postoperative state, it tends to subside with time (Fig. 3). In Table IV the present status of the extremities of the patients in this series is shown. Edema was graded 1 plus if there was slight swelling of the ankle, existing for a long time but not requiring any change in size of the hose or shoes. Patients were considered to have 2 plus edema if swelling, no higher

Fig. 1. Fig. 2.

Fig. 1.—Condition of extremities five months after ligation of vena cava and hysterectomy. Patient never had any edema of extremities.

Fig. 2.—Condition of extremities five years after ligation of vena cava and hysterectomy. Patient had four plus edema of left leg and two plus edema of right leg, preoperatively. This is one of the two patients having persistent two plus edema.

than the middle of the leg, occurred after walking a bit and regressed after lying down. The same circumstances cause 3 plus edema except that the swelling is up to the knee. Patients with 4 plus edema have swelling of the entire extremity. Forty-eight patients have had no edema at any time. Eight patients notice occasional mild swelling of the feet after they have been up and about for many hours. However, edema of the ankle or leg is not noticed. Six patients may be said to have true edema, in that some swelling of the ankle and lower half of the leg to about the calf is noted except when at complete bed rest. None of these patients are incapacitated in any manner.

Of the 6 patients with edema, 3 had 4 plus edema prior to ligation of the inferior vena cava, one had severe varicosities of the legs with ankle edema, and 2 had edema only after ligation. Retrograde thrombi occasionally developed but responded readily to lumbar sympathetic block. In nearly all our patients the right or left lumbar sympathetic chains, or both, were severed at the time of ligation, or lumbar sympathetic blocks were performed postoperatively on the uninterrupted side or sides. We believe that such procedures are valuable adjuncts in relieving the arterial and venous spasm occasioned by ligation of a large venous trunk and the absence of any severe postoperative complication in the legs is in no small part due to these precautionary measures. We have not noted any difference between patients in whom the vena cava was ligated in continuity or those in whom it was ligated and divided nor have we noted the development of phlegmasia cerulea dolens, though this has been reported by Veal.[9]

Fig. 3.—Condition of extremities nine years after ligation of vena cava.

The vascular status of an unselected group of patients was evaluated by Burch and associates[10, 11] of the Department of Medicine, Tulane University. They ascertained that circulation time from foot to heart, measured by means of a radioactive isotope, was variable but within normal limits in the patients studied. Venous pressure determinations on the veins of the lower extremities performed by members of both the Department of Medicine and the Department of Obstetrics and Gynecology varied from low normal values (120 mm. of

water pressure) to exceedingly high values (over 500 mm. of water). In the initial determinations few fell within normal limits and in the same patients there were differences in pressure in the two sides. With time there is a decline in pressures toward normal and in a number of instances to within normal limits (Fig. 4).

As stated previously, edema of the lower extremities is usually present immediately after operation, but it does not always occur, nor is the degree of edema related to venous pressures (Fig. 5). In some, edema was pronounced with moderate or relatively low pressures; in others with high pressures there was no edema. In still others the edema which was present initially regressed or disappeared without a change in venous pressure. Venous pressure and tissue pressure increases occurred concomitantly, a fact which would tend to

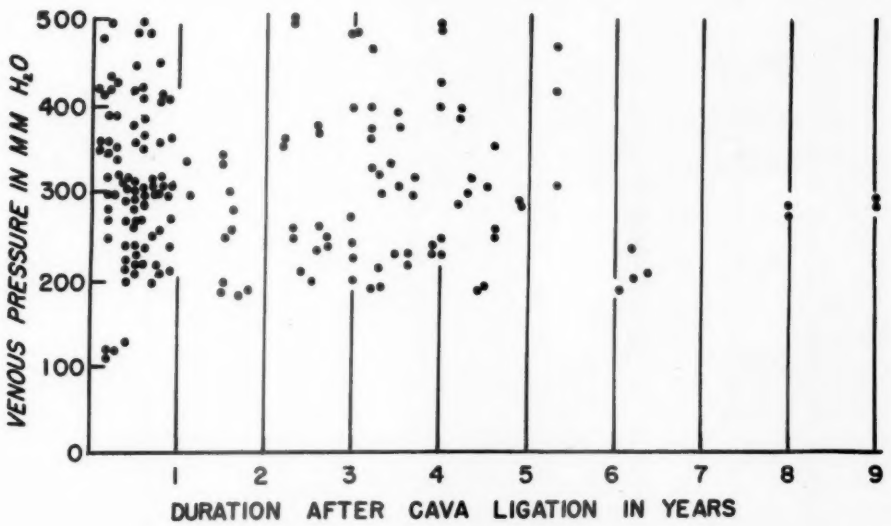


Fig. 4.—Spot graph showing venous pressure studies.

decrease the formation of edema. Plethysmographic studies of the toes indicated that pulsations were within normal limits though somewhat reduced and that on limbs to which the sympathetic chain had been interrupted the pulse deflections were increased.[8, 11] DeCamp and co-workers[12, 13] have observed persistent ambulatory venous hypertension in the legs of some patients studied postoperatively, again in the absence of significant clinical symptoms other than mild ankle edema. These observations, though not clearly defining all the circulatory adjustments, do indicate that there is adequate compensation for vena cava ligation.

ADDITIONAL SURGICAL PROCEDURES AT TIME OF LIGATION

Ligation of the inferior vena cava, whether performed by the transabdominal or extraperitoneal route, is a relatively simple procedure and is not accompanied by any degree of shock. Many patients had the right or left lumbar sympathetic chain, or both, sectioned at the same time as ligation. In

a few, unilateral salpingo-oophorectomy for severe thrombosis and infection of the ovary was necessary. Bilateral cystic ovaries necessitated bilateral salpingo-oophorectomy in 1 patient. In 5 cases hysterectomy was done at the same time, either because it was planned or because it was necessitated by the pathologic conditions (Table V) encountered. In another patient, nephrectomy was necessitated by an ectopic kidney on the right side with the thrombus extending into the renal vein. There was 1 death in this group as a result of a transfusion reaction (A. B., Table II). There was no increase in morbidity. In another case, the thrombus extended from the right ovarian vein into the cava, cephalad, past the confluence of the right and left renal veins. In this case the thrombus was "milked" caudad, and the right ovarian vein and 2 cm. of the inferior vena cava, just caudad to the confluence of the right renal vein, were resected. Recovery was immediate and uncomplicated.[14]

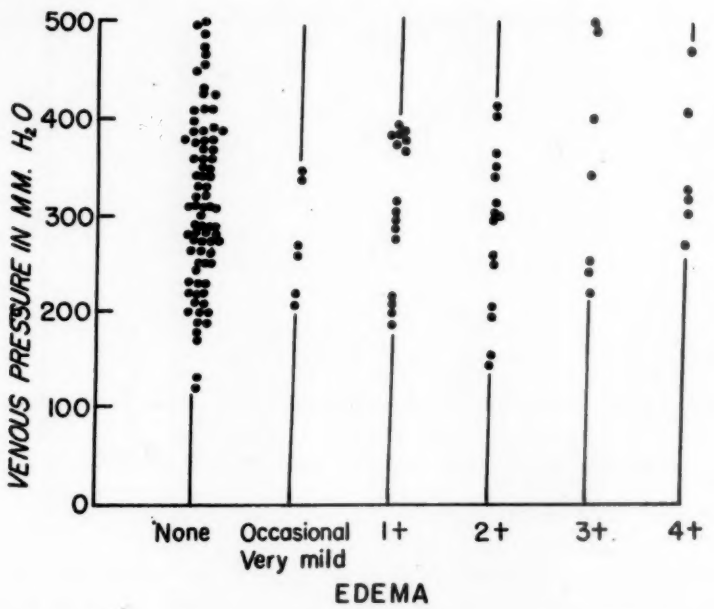


Fig. 5.—Spot graph showing relation of venous pressure to edema.

SUBSEQUENT SURGICAL PROCEDURES

In 16 patients subsequent surgical procedures were necessary (Table VI), either as a result of pelvic infection or development of disease after, but unrelated to, vena cava ligation. In 8 patients, hysterectomy was performed months to years following ligation. The indications for hysterectomy in these cases are listed in Table VI. At the time of hysterectomy no more bleeding was encountered than at average routine abdominal hysterectomy. The pelvic vessels were not engorged, congested, or varicosed, a fact which indicates that the venous return was adequate. In the patients having suspension of the uterus and repeated cesarean sections, there was no evidence of abnormal, disturbed vascularity. Two patients required lobectomy for residuals of the

original infarctions which had necessitated ligation of the vena cava. One died at the time of lobectomy as a result of hemorrhage from the operative field; the other is well today. In 2 patients, severe burns of the legs healed with appropriate therapy indicating normal tissue metabolism.

TABLE IV. DEVELOPMENT OF EDEMA AFTER LIGATION OF INFERIOR VENA CAVA FOR SUPPURATIVE PELVIC THROMBOPHLEBITIS

EDEMA	CASES
None	48
Mild	8
1 plus	4
2 plus	2
3 plus	0
4 plus	0
Died in hospital	8
Total	70

TABLE V. HYSTERECTOMY AT TIME OF VENA CAVA LIGATION FOR PELVIC SUPPURATIVE THROMBOPHLEBITIS

PATIENT	OPERATION	PATHOLOGY
M. A.	5/25/46	Acute suppurative pelvic thrombophlebitis; partially retained placenta
J. D.	12/10/48	Chronic suppurative pelvic thrombophlebitis; severe dyspareunia; badly lacerated cervix with endocervicitis
E. W.	2/ 5/46	Acute suppurative pelvic thrombophlebitis; uterine fibroids
H. W.	12/31/48	Acute suppurative pelvic thrombophlebitis; gangrene of uterus
A. B.	8/31/48	Fibroids; chronic suppurative pelvic thrombophlebitis

CONDITION OF VULVA, VAGINA, AND RECTUM

In none of the patients did varicosities, discoloration, or edema of the vulva, vagina, or cervix develop. The only pathologic alterations noted in these structures at follow-up examinations were those resulting from parturition or infection. No hemorrhoidal masses were observed nor did any patient complain of hematuria. No case of vaginal discharge could be attributed to "pelvic congestion."

As stated previously, 8 patients have had subsequent hysterectomies for symptomatic residuals of the pelvic infection or uterine fibroids. In none was hysterectomy performed for menstrual irregularities alone. In the remaining patients who have uteri, the menstrual pattern is the same as prior to ligation of the vena cava and ovarian vessels. A study of these patients as regards ovulation, pregnancy, and parturition will be reported at a later date.

CONCLUSIONS

1. Ligation of the inferior vena cava and ovarian vessels is indicated in patients with suppurative pelvic thrombophlebitis who fail to respond to medical therapy, regardless of the severity of the illness.

2. Ligation of the inferior vena cava and ovarian vessels in critically ill patients is associated with a negligible mortality rate. The deaths reported in

TABLE VI. SURGICAL PROCEDURES AFTER LIGATION OF VENA CAVA FOR SUPPURATIVE PELVIC THROMBOPHLEBITIS

PATIENT	VENA CAVA LIGATED	SUBSEQUENT OPERATION	INDICATIONS	RESULTS
H. W.	12/31/48	Skin graft 2/12/49	Third degree burn left thigh, donor site right thigh	Healed 2/28/49, asymptomatic
M. B.	10/30/44	Compression bandages 12/19/44	Second degree burn, entire left leg	Healed, asymptomatic
G. A.	4/ 7/48	Dilatation and curettage 11/9/48	Bleeding retained secundines	Asymptomatic
M. S.	5/25/46	Dilatation and curettage 11/26/46	Polymenorrhea, endometrial hyperplasia	Asymptomatic
J. D.	'42	Lobectomy '44	Lung abscess, residue of infarct	Died
E. P.	6/18/47	Lobectomy 6/30/47	Gangrene of lung, residue of infarct	Asymptomatic
E. W.	9/ 1/42	Laparotomy and plastic 3/3/46	Birth injuries, sterilization	Asymptomatic
D. P.	1/13/45	Cesarean section (2) 11/4/48 and 11/6/50	Previous cesarean section	Asymptomatic
D. S.	8/29/48	Hysterectomy 8/29/48	Severe dyspareunia, chronic endocervicitis	Asymptomatic
P. H.	4/25/42	Hysterectomy 7/9/48	Pelvic pain, bilateral tubo-ovarian abscess	Asymptomatic
O. D.	5/ 2/42	Hysterectomy 7/30/42	Large fibroid	Asymptomatic
A. L.	4/30/42	Hysterectomy 6/15/47	Lower abdominal pain, chronic cervicitis, chronic bilateral salpingitis	Asymptomatic
H. K.	1/ 7/49	Hysterectomy 5/31/49	Dyspareunia, parametritis, prolapse of uterus	Asymptomatic
D. H.	10/24/49	Hysterectomy 7/14/50	Bilateral tubo-ovarian abscess	Asymptomatic
I. A.	12/15/49	Hysterectomy 4/24/51	Chronic cervicitis, salpingo-oophoritis	Asymptomatic
D. St. J.	3/15/49	Hysterectomy 2/17/51	Chronic cervicitis, salpingo-oophoritis, tubo-ovarian abscess	Asymptomatic

this series resulted from the delay in operating or from the underlying pathologic condition and not from the operation itself.

3. Subsequent surgical procedures performed on these patients were not the result of ligation of the vena cava and ovarian veins.

4. The operative hazard is not increased in patients who have had previous vena cava ligation and who require surgical procedures later.

5. The vena cava can be ligated at the same time as other surgical procedures are being performed.

6. In our series, no patient was incapacitated. Adequate compensation for the circulation in the extremities followed ligation.

7. Menstrual or sexual function was not altered by ligation of the inferior vena cava and ovarian vessels.

REFERENCES

1. Collins, C. G., MacCallum, E. A., Nelson, E. W., Weinstein, B. B., and Collins, J. H.: Suppurative Pelvic Thrombophlebitis: A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Vessels. I. Incidence, Pathology, and Etiology, SURGERY 30: 298, 1951.

2. Collins, C. G., Nelson, E. W., Collins, J. H., Weinstein, B. B., and MacCallum, E. A.: Suppurative Pelvic Thrombophlebitis: A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Vessels. II. Symptomatology and Diagnosis, SURGERY 30: 311, 1951.
3. Collins, C. G., and Ayers, W. B.: Suppurative Pelvic Thrombophlebitis: A Study of 70 Patients Treated by Ligation of the Inferior Vena Cava and Ovarian Vessels. III. Surgical Technique, SURGERY 30: 319, 1951.
4. Northway, R. O., and Greenway, G. D.: The Vena Cava and Its Collateral Circulation, Univ. Hosp. Bull., Ann Arbor 10: 67-69, 1944.
5. Keen, J. A.: Collateral Venous Circulation in Case of Thrombosis of Inferior Vena Cava, and Its Embryological Interpretation, Brit. J. Surg. 29: 105-114, 1941.
6. Batson, O. V.: The Role of the Vertebral Veins in Metastatic Processes, Ann. Int. Med. 16: 38-45, 1942.
7. Robinson, L. S.: The Collateral Circulation Following Ligation of the Inferior Vena Cava, SURGERY 25: 329-347, 1949.
8. Collins, C. G., Nelson, E. W., Ray, C. T., Weinstein, B. B., and Collins, J. H.: Ligation of the Vena Cava and Ovarian Vessels, Am. J. Obst. & Gynec. 58: 1155-1168, 1949.
9. Veal, J. R., Dugan, T. J., Jamison, W. H., and Bauersfeld, R. S.: Acute Massive Venous Occlusion of the Lower Extremities, SURGERY 29: 355-364, 1951.
10. Burch, G. E., and Winsor, T.: Physiological Studies on 5 Patients Following Ligation of the Inferior Vena Cava, Proc. Soc. Exper. Biol. & Med. 53: 135-138, 1943.
11. Ray, C. T., and Burch, G. E.: Vascular Responses in Man to Ligation of the Inferior Vena Cava, Arch. Int. Med. 80: 587-601, 1947.
12. DeCamp, P. T., Schramel, R. J., Ray, C. J., Feibleman, N. D., Ward, J. A., and Ochsner, A.: Ambulatory Venous Pressure Determinations in Postphlebitic and Related Syndromes, SURGERY 29: 44-70, 1951.
13. DeCamp, P. T., Ward, J. A., and Ochsner, A.: Ambulatory Venous Pressure Studies in Postphlebitis and Other Disease States, SURGERY 29: 365-380, 1951.
14. Collins, J. H., Baggs, W. J., and Ball, R. C.: Partial Excision of the Inferior Vena Cava in Suppurative Pelvic Thrombophlebitis, New Orleans M. & S. J. 103: 288-290, 1951.

INTUSSUSCEPTION IN ADULTS

Report of 15 Cases

Charles H. Brown, M.D., and Arthur G. Michels, M.D., Cleveland, Ohio

(From the Cleveland Clinic and The Frank E. Bunts Educational Institute)

INTUSSUSCEPTION in older children and adults differs in many respects from the conditions seen in infants. Eliot and Corscaden,[1] in 1911, were able to collect 300 cases from the literature, and Donhauser and Kelly[2] collected 665 reviews from the American and English literature from 1900 through 1947. Nevertheless, the former condition is relatively uncommon, and individual case reports still appear. Nichols[3] reports that 75 per cent of the cases of intussusception occur in infants under two years of age.

While intussusception in children is frequently "primary" or without any apparent cause or disease of the bowel, this condition in adults is usually secondary to some disease of the intestines. Christopher[4] reviewed 43 cases due to benign, and 16 due to malignant, tumors. Donhauser, in reporting on 665 patients, found 213 had benign tumors, 123 had malignant tumors, 43 cases were associated with a Meckel's diverticulum, and 27 patients had a pre-existing gastroenterostomy. Only 158 were instances of primary intussusception in adults in this collected series. The remaining had a variety of other causative factors.

Intussusception in children is usually acute, but in adults it is frequently chronic and intermittent. The patient's story suggests intermittent and recurrent small bowel obstruction in contrast to the acute catastrophic form seen in infants. In addition, the symptoms in the adult may be confused by those symptoms caused by the primary disease (i.e., tumor).

The treatment of acute intussusception in infants differs from the treatment of chronic intermittent intussusception in adults. Because this condition in infants is usually primary, it may be reduced by enemas under a little pressure. Enemas may also reduce an intussusception in adults but, unless the underlying cause is removed, it may recur.

The differences between intussusception in infants and adults are tabulated in Table I.

Since intussusception in adults is relatively uncommon, and presents a different clinical picture than in children, we have reviewed our cases at the Cleveland Clinic.

RESULTS

During a period in which 430,000 new patients were registered at the Cleveland Clinic, only 15 cases of adult intussusception were recorded.

The fact that intussusception in adults is usually secondary to some other disease is corroborated by our observations that 14 of our 15 cases were secondary

Received for publication, July 21, 1951.

to tumors. Only 1 of the 15 patients had an apparent "primary" intussusception. There were 8 malignant tumors, 6 of which were carcinoma and 2 of which were sarcoma. The remaining 6 had benign tumors, 5 being lipomas and 1 a large papilloma of the cecum. Nichols[3] reported that 70 per cent of cases of adult intussusception are secondary to other conditions such as tumor, diverticulosis, and ulcer. In any adult with intussusception it is imperative that a strenuous effort be made to diagnose the underlying cause.

TABLE I. DIFFERENCES BETWEEN INTUSSUSCEPTION IN INFANTS AND ADULTS

	INFANTS	ADULTS
Incidence	Common	Uncommon
Etiology	Primary—not associated with other gastrointestinal disease	Secondary—to benign and malignant tumors, Meckel's diverticulum, preexisting gastroenterostomy, etc.
Clinical picture	Acute onset	Chronic intermittent course, suggesting recurrent bowel obstruction
Physical examination	Mass almost always palpable	Mass palpable in only ⅓ to ½ of the cases
X-ray	Usually characteristic "coiled spring" appearance, obstruction, and small barium column in intussusceptum	Findings may be similar to that in infants, but intussusception may not be present at time of x-ray examination and findings may be masked by tumor, etc.
Treatment	May be reduced by enema with pressure; surgery necessary only when enema is unsuccessful	If reduced by enema, recurrences frequent; surgery usually necessary because the underlying cause is still present

1. Clinical Picture.—This group of patients is too small to attach significance to the sex ratio of 9 men to 6 women, or to the average age of 48. The youngest patient was 20, while the oldest was 63 years of age.

The clinical features are presented in Column 1 of Table II. The most frequent complaint was abdominal cramps which were present in 9 of the patients. Eight had acute but intermittent and recurrent attacks of abdominal pain and cramps, suggesting repeated episodes of bowel obstruction. Six complained of loss of weight, and 6 of blood in the stool. Five patients had diarrhea, which was intermittent. Four complained of vomiting associated with the attacks, while 3 had abdominal distention. One complained of anorexia and one of a false urge to defecate. The duration of symptoms in this group varied from 3 days in one patient to 3 years in another, the average being 8.2 months. From a review of the symptoms in our group, it can be seen that the adult with intussusception most frequently presents a history suggestive of recurrent attacks of bowel obstruction.

A mass usually is palpable in the infant with intussusception. In our group a mass was palpated in only 6 of the 15 cases. This may be because of the increased muscular development in the adult which makes palpation more difficult.

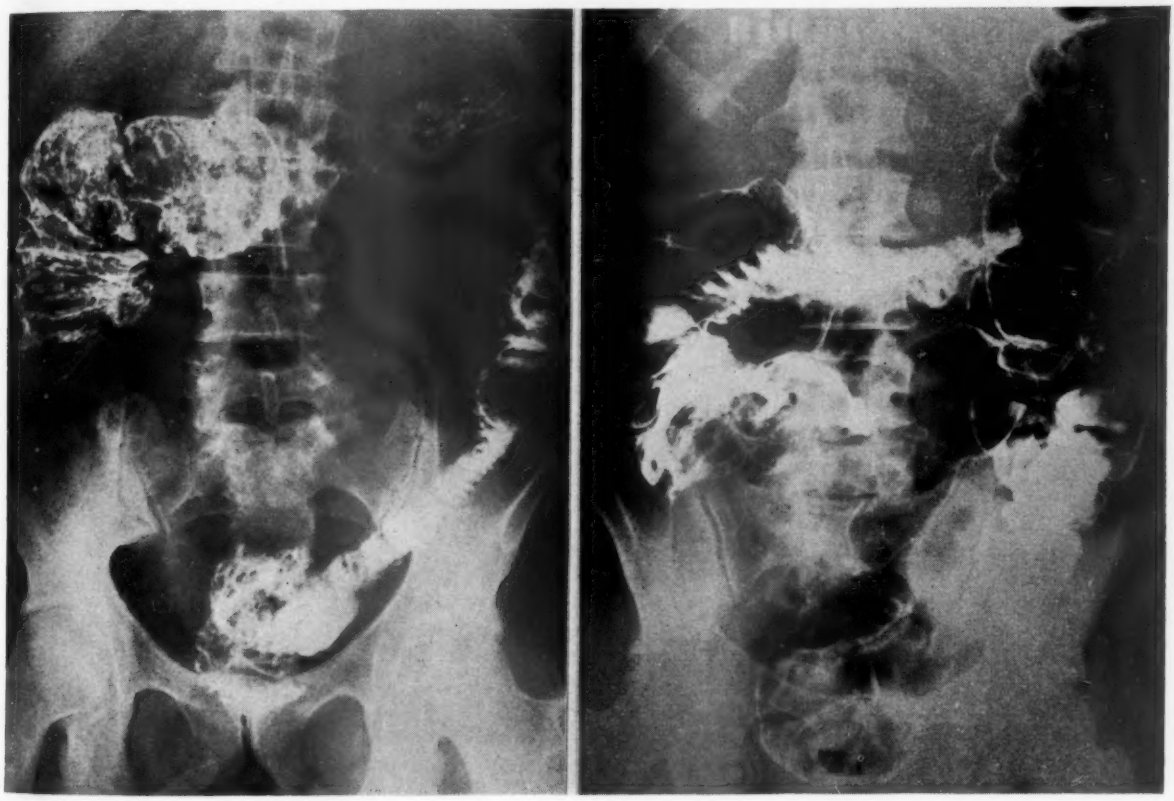
The four cardinal signs of intussusception in both adults and children are: (1) abdominal cramps, (2) vomiting, (3) a palpable mass, and (4) passage of blood by rectum. Vomiting was a symptom in only 4 of our patients, although Ferrer[5] reported vomiting in 17 of his 25 cases.

TABLE II. FINDINGS IN CASES OF INTUSSUSCEPTION

CASE	CLINICAL PICTURE	X-RAY EXAMINATION	OPERATIVE FINDINGS	OPERATION	PATHOLOGY
1	Mass, weight loss, weakness, anorexia—1 yr.	Polypoid mass; intussusception	Cecal tumor; intuss.	Right colectomy	Polypoid mucinous ca.
2	Diarrhea, bloody stools, intermittent cramps —5 mo.	Barium enema and small bowel negative	Not done	Not done	(Died 2 mo. later) Autopsy: melanosarcoma of jejunum with intuss.
3	Attacks of nausea, vomiting, cramps, diarrhea—2 mo.; mass	Intuss. and tumor	Intuss. and cecal tumor	Obstructive resection	Mucinous polypoid adenoca. of cecum
4	Cramps and distention, loss 20 lbs.—3 mo. bloody stools—3 wk.	Intuss. with polypoid tumor	Intuss. and tumor	Right colectomy; x-ray Rx.	Lymphosarcoma (alive and well 7 yr. later)
5	Cramps, constipation, loss 37 lbs.—6 mo.; hard fixed mass	Filling defect	Intuss. with ca. of cecum	Right colectomy	Ulcerating ca. of cecum
6	Intermittent attacks of anorexia, distention, lower abdominal pain —1 yr.	Filling defect, sigmoid	Pedunculated ca.; intuss. into rectosigmoid	Resection of sigmoid	Ca. of sigmoid
7	Proctorectal mass—ca.; intermittent lower abdominal cramps, vomiting, loss 15 lbs.	Filling defect and (?) intuss.	Intuss. and tumor	Right colectomy	Ca. of cecum
8	Bloody and tarry stools —6 wk.; mass	Intuss.; mass	Intuss. with ca. of transverse colon	Obstructive resection	Adenoca. of transverse colon
9	Daily cramping, upper abdominal distress, vomiting, loss 25 lbs. —3 mo.	Annular lesion; (?) splenic flexure	Intuss. with tumor	Right colectomy	Lipoma of cecum, 5 by 6 cm.
10	Recurrent attacks of cramps, diarrhea—5 mo.	Intuss. with obstruction; tumor	Intuss. with tumor	Obstructive resection	Lipoma of ascending colon
11	Acute attacks of colicky epigastric pain, constipation, loss 50 lbs. —6 mo.	Not done	Intuss. of ileum; no tumor	Unable to reduce intuss., ileocecostomy	Intuss. primary (?)
12	Intermittent cramps—6 mo.; vomited once	Partial obstruction and intuss.; tumor	Intuss.; tumor	Right colectomy	Lipoma; hepatic flexure
13	Bouts of diarrhea, abdominal cramps, distention, blood in stools, loss 35 lbs.—1 yr.	Polypoid lesion of cecum with intuss.	Ileocecal intuss. with tumor	Right colectomy	Benign papilloma of cecum
14	Intermittent false urge to defecate—6 mo.; bloody stools—3 days; mass	Obstructive mass of sigmoid with intuss.	Tumor and intuss.	Resection of sigmoid	Large polypoid submucous lipoma
15	Attacks of diarrhea, pus, blood in stool—3 yr.; recent attack—3 wk.	Obstructive mass of descending colon; no indication intuss.	Intuss. lipoma	Transcolonic excision	Lipoma of descending colon

2. Diagnosis.—The diagnosis of intussusception in the adult is frequently difficult because of the chronicity and intermittency of the symptoms, and because the symptoms of the intussusception may be masked by the underlying disease. The difficulty of diagnosis is well demonstrated by the fact that 2 of

our patients had had appendectomies performed elsewhere two months before admission to the Cleveland Clinic. The appendectomies did not, of course, relieve their symptoms. The diagnosis of intussusception in the adult is rarely made preoperatively on clinical bases, but may be determined by roentgen study. Schatzki[6] has outlined the roentgenologic features of intussusception both in films of the abdomen and on barium enema examination. He demonstrated that the "coiled spring" appearance is pathognomonic, and is produced by barium insinuated between the intussusceptum and the intussuscipiens. Other roentgenologic features are: absence of normal gas pattern on the flat film, a narrow column of barium in the intussusception suggesting Kantor's "string sign" of regional ileitis, and evidence of obstruction to the flow of barium.



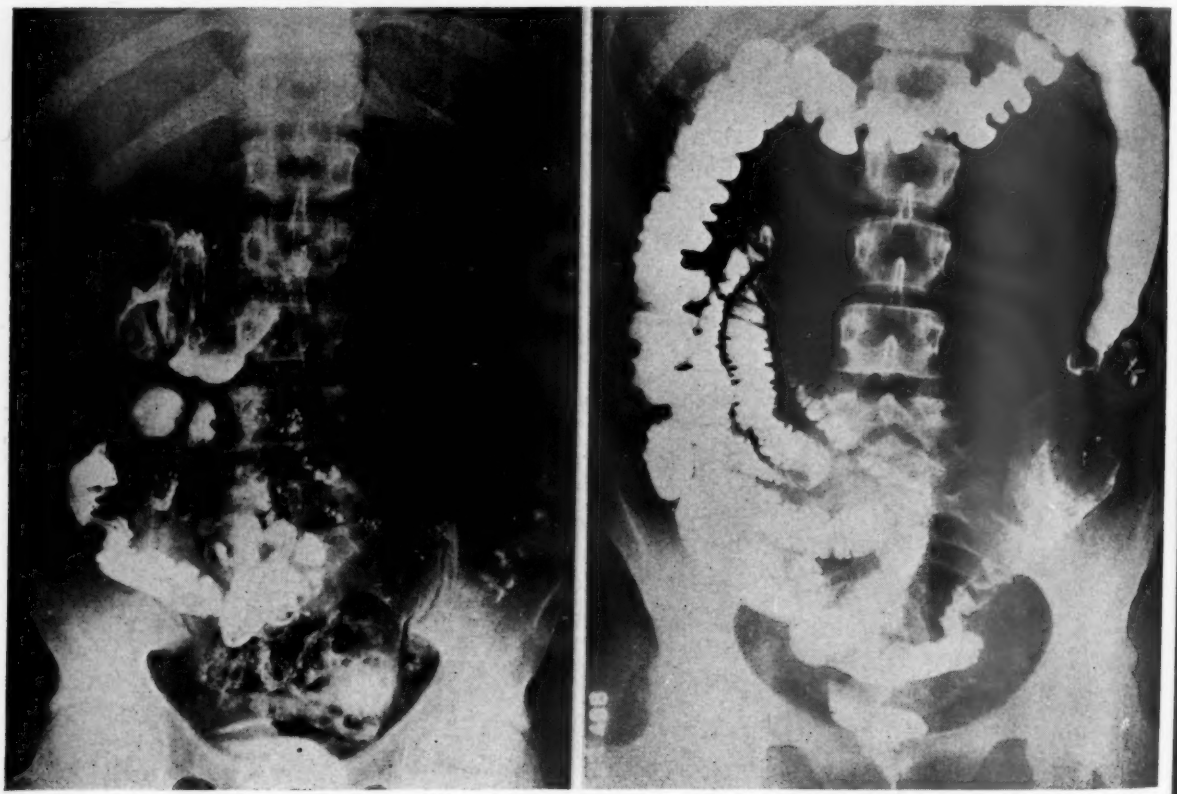
A. *B.*

Fig. 1.—*A*, Typical "coiled spring" appearance of intussusception, caused by benign adenoma of cecum. *B*, Suggestive "coiled spring" appearance of intussusception, caused by polypoid carcinoma of cecum.

Diagnoses of tumor and intussusception were made in 8 instances, and a tumor with probable intussusception in 1 patient. In 4 cases a filling defect was evident on the barium enema study, but no signs of intussusception were present. It must be remembered that intussusception is frequently intermittent and may be absent at the time of, or reduced by, the barium enema examination, but may be present later at surgery. Barium enema examination was not done in 1 patient admitted during an acute attack. The examination was negative, as were

roentgenograms of the small bowel, in 1 patient having a melanosarcoma of the jejunum that resulted in intussusception.

3. Treatment.—It has been demonstrated that intussusception in children frequently is reduced by the hydrostatic pressure of an enema, or by barium enema examination, and that the intussusception does not usually recur. Hipsley[7] reported that hydrostatic pressure was effective in reducing 60 per cent of his cases; he successfully reduced the intussusception in 90 of 142 cases by this method. Miller[8] and others have corroborated these findings on this type of treatment of intussusception in children.



A. *B.*

Fig. 2.—*A*, Obstruction with "string sign" due to barium entering intussusceptum. Caused by benign adenoma of cecum. *B*, Large tumor of descending colon demonstrated by barium enema with no evidence of intussusception. At operation intussusception was revealed, due to large lipoma of descending colon.

In adults, however, an intussusception reduced by the foregoing measures is almost certain to recur unless the underlying cause is removed. Surgery is almost always necessary in adults with intussusception. Reduction before surgery may enable the roentgenologist to demonstrate the cause of the intussusception, and may facilitate the surgeon's task. Only 1 of our patients was not subjected to surgery; in that instance, a diagnosis of melanosarcoma of the jejunum with intussusception was not established until autopsy examination 2 months later.

Resections with primary anastomoses were performed in 9 patients, while obstructive resections were done in 3. A transcolonic excision of a lipoma in the descending colon, which had caused a reducible intussusception, was done in 1 patient. The surgeon was unable to reduce the intussusception in the patient who apparently had a primary intussusception. An ileocecostomy was done to by-pass the intussusception in this instance. In the entire group of patients there was no operative mortality.

SUMMARY

The differences between acute intussusception in infants and chronic recurrent intussusception in adults has been discussed.

Fifteen adults with intussusception have been observed at the Cleveland Clinic, indicating the low incidence of this condition. Fourteen patients had tumors which caused the intussusceptions, the tumors being malignant in 8 and benign in 6.

The clinical manifestations in these patients were intermittent, recurrent attacks of abdominal pain and cramps, suggesting repeated episodes of bowel obstruction. Cramps, vomiting, presence of a palpable mass, and passage of blood by rectum are the basic signs of intussusception. The diagnosis of intussusception is rarely made in the adult, clinically, but may be determined by roentgenologic examination.

The treatment of the adult patient with intussusception is surgical, with excision of a benign tumor, or resection, since this is the only method that removes the cause.

REFERENCES

1. Eliot, E., Jr., and Corscaden, J. A.: Intussusception, With Special Reference to Adults, Ann. Surg. **53**: 169, 1911.
2. Donhauser, J. L., and Kelly, E. C.: Intussusception in Adults, Am. J. Surg. **79**: 673, 1950.
3. Nichols, H. G.: Intussusception in Adults; Consideration of Therapeutic Measures and Case Report, Surg., Gynec. & Obst. **73**: 832, 1941.
4. Christopher, F.: Intussusception in Adults; 2 Additional Cases, Surg., Gynec. & Obst. **63**: 670, 1936.
5. Ferrer, J. M., Jr.: Symposium on Surgical Emergencies; Intussusception in Children and Adults, S. Clin. North America **30**: 515, 1950.
6. Schatzki, R.: Roentgenologic Appearance of Intussuscepted Tumors of Colon, With and Without Barium Enema Examination, Am. J. Roentgenol. **41**: 549, 1939.
7. Hipsley, P. L.: Treatment of Intussusception, SURGERY **1**: 825, 1937.
8. Miller, E. M.: Acute Intussusception, Ann. Surg. **98**: 796, 1933.

THE CONSERVATIVE TREATMENT OF THE ACUTE FORM OF SIGMOID VOLVULUS

NORMAN H. ISAACSON, M.D., AND DAN B. GREER, M.D.,* WASHINGTON, D. C.

(From the George Washington Surgical Service, Gallinger Municipal Hospital)

IN THE United States, volvulus of the sigmoid colon is so uncommon (comprising between 1 and 4 per cent of all intestinal obstruction[1-3, 5]) that few series are large enough to evaluate adequately the clinical picture, diagnosis, and therapy of this condition. As a consequence, many methods of treatment of this condition have been advocated by American authors: (1) *Simple detorsion* of the twisted loop at operation[1, 4] (if the bowel is not gangrenous) carries the lowest mortality rate, but unfortunately, the volvulus recurs in 20 to 30 per cent of the cases,[1-7, 9] This has led to a variety of methods that attempt to tack the loop of bowel to the abdominal parietes, a procedure which has been largely unsuccessful in preventing recurrence. Sigmoidostomy,[10] in a like attempt to fix the bowel to the abdominal wall, is not accepted by most authorities.[4] (2) *Cecostomy,*[3, 4] although it is occasionally followed by spontaneous detorsion of the sigmoid volvulus, is a completely irrational procedure. It is usually performed without adequate exploration of the sigmoid colon for possible circulatory changes and is usually unsuccessful in relieving what is essentially a closed loop obstruction. (3) *Obstructive resection* by either the Rankin or Mikulicz methods, while occasionally advocated for the treatment of the viable loop of sigmoid after detorsion,[10] is usually reserved for those cases where gangrene has occurred.[1, 4, 26] The disadvantages of a temporary colostomy, prolonged hospitalization, and secondary operation, make it undesirable except where necessity dictates. (4) *Primary resection* with end-to-end anastomosis[12, 13] has recently been tried. It necessitates doing an anastomosis in the presence of an unprepared bowel, but with the use of the present-day antibiotics it entails somewhat smaller risk than in former years.

In the hands of the surgeons of the United States the mortality rate from sigmoid volvulus has ranged from 25 to 60 per cent[1-4, 8] perhaps more due to delay in diagnosis than to choice of operative procedure.

In contrast to the limited experience of American surgeons with sigmoid volvulus, that of the practitioners in Eastern Europe and the Scandinavian countries is a large one. In this area of the world, volvulus comprises 23 to 50 per cent [14-16] of all cases of intestinal obstruction and 60 to 75 per cent of these occur in the sigmoid. The markedly increased incidence in this segment of the world population has been attributed to national dietary habits and to racial anatomic differences in the length of the sigmoid loop.[14]

With their large experience with this type of lesion, the Scandinavian surgeons gradually evolved a method of decompression of the twisted loop of

Received for publication, Aug. 24, 1951.

*Present address, Veterans Administration Hospital, Cheyenne, Wyo.

sigmoid colon from below. There had been many isolated reports in the literature of accidental reduction of sigmoid volvulus by barium enema or by proctoscopy, but the method of consciously attempting this reduction by means of a rectal tube was probably first suggested by Laurell[17] and first done successfully by Nørgaard.[18, 19] Experience with this method rapidly grew in these countries so that Bruusgaard,[20] on a visit to this country in 1947, was able to report on 91 cases in which rectal tube decompression was performed 168 times with a mortality rate of 14.2 per cent (7.7 per cent of treatment). Since then Michel and McCafferty[4] reported using this method in four cases with one fatality (in which unrecognized gangrene of the bowel wall was present) and Wangensteen used it in two cases.[20] Two weeks following decompression, Wangensteen resected the redundant loop of sigmoid after the bowel had been adequately prepared, a course of attack which appears to be the most logical in view of the known tendency to recurrence.

Seven cases of sigmoid volvulus reduced from below by accident or design will be presented, and the indications, contraindications and technique of this method of treatment discussed.

CASE REPORTS

CASE 1.—S. M., a 38-year-old Negro man, was admitted to Gallinger Municipal Hospital on Jan. 11, 1949, with a history of recurrent bouts of crampy abdominal pain of many years duration. Attacks occurred approximately 2 to 3 times yearly, usually lasted one day and were relieved by Epsom salt cathartics. When relieved, attacks were always terminated by the expulsion of much gas or fecal matter. On the day of admission the attack occurred as usual but was not relieved by Epsom salts and the pain increased in severity. Nausea without vomiting was present.

When the patient was admitted, the abdomen was markedly distended and tympanitic with hyperactive peristalsis. No tenderness or rigidity was present. A flat plate of the abdomen showed a volvulus of the sigmoid colon. A rectal tube was passed through a proctoscope and considerable amounts of gas and liquid feces were expelled. The patient became asymptomatic. While in the hospital the patient experienced several attacks of mild cramping abdominal pain (the rectal tube had been removed) but these subsided spontaneously. A barium enema on January 19 showed what was reported as "segmental megacolon of the sigmoid flexture." Resection was advised, but the patient refused the operation and signed himself out against advice on Jan. 20, 1949. No further follow-up was possible.

CASE 2.—M. B., a 94-year-old Negro woman, was admitted to Gallinger Municipal Hospital on March 18, 1951, with a history of pain and swelling of the abdomen for about one week. She had been having occasional episodes of crampy pain for about two weeks, with increased severity one week prior to admission. She had small watery bowel movements up to three days previously when constipation ensued. Vomiting occurred several times in the twenty-four hours before she came to the hospital.

On examination, the abdomen was found to be markedly distended but soft. An x-ray examination of the abdomen showed the typical picture of volvulus of the sigmoid colon (Fig. 1).

A proctoscope was inserted and resulted in an immediate gush of soft feces and gas. A soft rectal tube was inserted for a distance of 25 cm. and securely strapped to the anus with adhesive tape. The abdomen deflated like a punctured balloon and postreduction films showed adequate reduction of the distended sigmoid (Fig. 2).

The patient appeared to be doing well postreduction and was tolerating a soft diet when she suddenly died on March 20, 1951. Post-mortem examination showed the cause of

death to be pulmonary embolism, probably from an unrecognized phlebothrombosis of the femoral veins. There was an asymptomatic gastric carcinoma without metastases. The sigmoid loop was redundant but had been completely reduced and was viable.

CASE 3.—M. M., a 47-year-old Negro woman, was admitted to Gallinger Municipal Hospital on Feb. 19, 1951, with a history of intermittent abdominal cramps of twelve months' duration, severe abdominal cramps of two weeks' duration, and constipation, nausea, and vomiting for three days prior to admission.

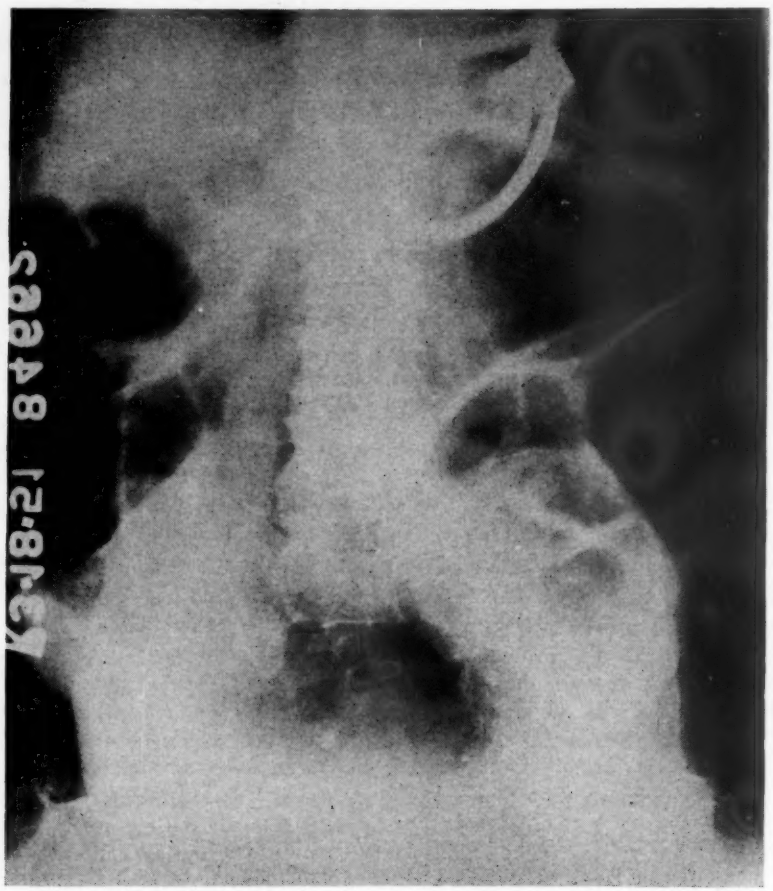


Fig. 1 (Case 2).—Flat plate of abdomen showing the tremendous distension of the sigmoid flexure extending almost to the diaphragm.

On examination the abdomen was found to be moderately distended with some tenderness in both lower quadrants. Flat plate of the abdomen showed a markedly distended loop of large bowel. The patient was proctoscoped and the examiner remarked that when the proctoscope was inserted to 25 cm. there resulted a gush of air that blew the eyepiece off the instrument. No other abnormalities were found.

The full significance of these findings was not appreciated and the abdomen was explored the same day through a right rectus incision. The sigmoid loop was redundant and somewhat edematous but not distended at operation. No other abnormalities were found within the abdominal cavity. An appendectomy was performed and the abdomen closed. The patient developed pneumonia and a wound dehiscence and was not well enough to be discharged until March 14, 1951, all because of an operation that was unnecessary. The volvulus had been adequately reduced preoperatively.

CASE 4.—R. A., a 35-year-old woman, was admitted to Gallinger Municipal Hospital on April 9, 1948. Three days prior to admission she had abdominal cramps which subsided in one hour without therapy. On the two succeeding days she took cathartics without success although she felt well. On the afternoon of admission she was again seized with severe periumbilical cramps which persisted. She was still constipated but passed small amounts of flatus. No vomiting occurred. She had a shaking chill just prior to admission.

On examination the abdomen was found to be moderately distended, with minimal tenderness throughout. Peristalsis was hyperactive with occasional rushes. A flat plate of the abdomen was consistent with a volvulus of the sigmoid colon.

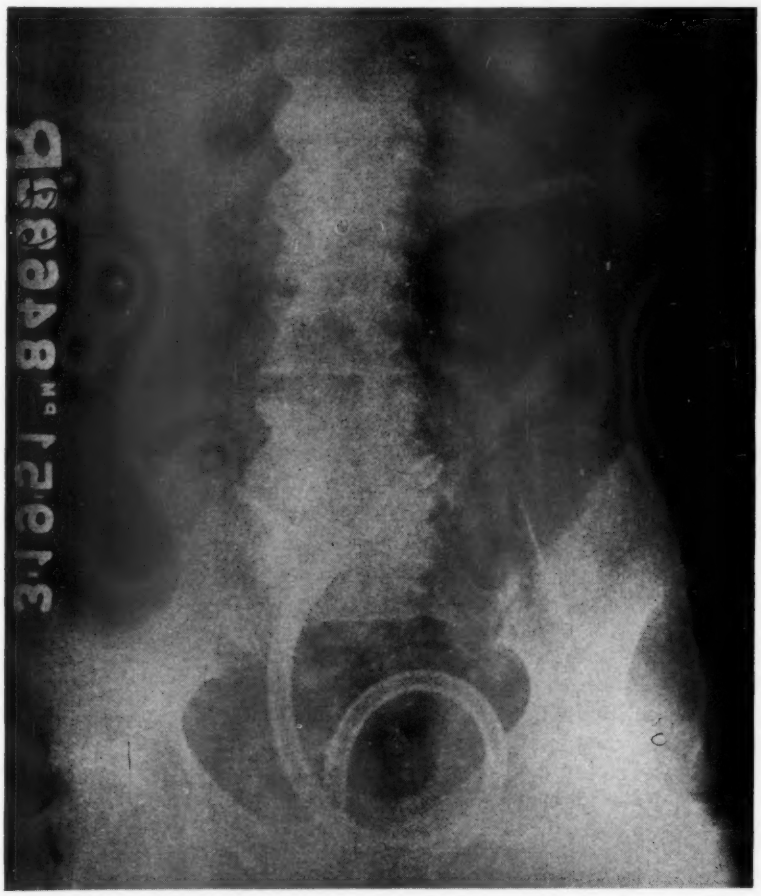


Fig. 2 (Case 2).—Postreduction film showing rectal tube in place and volvulus decompressed.

She was given a tap water enema (750 c.c.) with remarkable results. Immediately thereafter she was completely relieved of symptoms and a short while later had several liquid bowel movements of massive proportions.

A barium enema study five days later showed some redundancy of the sigmoid colon, but an operation was not recommended. She was discharged on April 19, 1948, and has been lost to follow-up.

CASE 5.—L. R., a 40-year-old Negro man, was admitted to Gallinger Municipal Hospital on April 17, 1948, complaining of abdominal cramps, constipation of three days' duration, and periumbilical pain and vomiting of seven hours' duration. No previous history of abdominal pain was given. There were no other gastrointestinal or genitourinary complaints. The abdomen was moderately distended but soft with some tenderness in the left

lower quadrant. A flat plate of the abdomen showed a distended loop of large bowel. An attempt at proctoscopy resulted in a gush of gas and liquid feces through the proctoscope and the patient was immediately relieved of all symptoms. He was discharged, asymptomatic, three days later and has been lost to follow-up.

CASE 6.—J. S., a 49-year-old Negro man, was admitted to Gallinger Municipal Hospital on Dec. 29, 1948, with a four-day history of abdominal cramps, anorexia, vomiting, and constipation. His record indicated a previous admission to his hospital in 1943 when he was operated on for large bowel obstruction and "nothing was found" at laparotomy. Review of his x-ray file, however, showed a typical preoperative picture of volvulus (which probably reduced spontaneously) and a postoperative barium enema showing dilatation of the entire large bowel (megacolon). From that admission in 1943 to this in 1948 he had frequent attacks of abdominal distension relieved by expulsion of gas.

On this admission the abdomen was moderately distended and tympanitic with hyperactive peristalsis. No tenderness or rigidity was present. Flat plate of his abdomen showed a volvulus of the sigmoid colon.

A rectal tube was inserted through a proctoscope and resulted in expulsion of a large amount of liquid feces and gas under pressure. The patient was completely relieved of symptoms.

A barium enema on Jan. 3, 1949, again revealed a megacolon. However, no operation was advised and the patient was discharged on Jan. 13, 1949.

Recently the patient has been admitted to another hospital in this city, apparently for a recurrence of his volvulus. Resection is contemplated. This case represents volvulus in a megacolon which is a not infrequent complication of that condition.[21-23]

CASE 7.—W. S., a 77-year-old Negro man, was admitted to Gallinger Municipal Hospital on July 23, 1951, with progressive abdominal distension of four weeks' duration associated with diarrhea up until one week prior to admission when obstipation ensued. There was no history of vomiting, melena, or tarry stools.

On examination the abdomen was found to be markedly distended and tympanitic with tinkling peristalsis audible. An x-ray examination of the abdomen showed the typical picture of sigmoid volvulus.

A proctoscope was inserted and resulted in the immediate expulsion of a tremendous amount of gas and liquid stool under pressure. A rectal tube was inserted through the proctoscope and resulted in further passage of feces. The rectal tube was strapped to the anus and kept in place several days. The abdominal distension rapidly disappeared.

Barium enema, on July 30, showed "marked distension of sigmoid flexure." No filling defects were noted.

Because of the advanced age and poor cardiac status of this patient, operation was not advised. The patient was discharged from the hospital asymptomatic.

DISCUSSION

In summary: seven patients with sigmoid volvulus have been presented, all of whom had successful reduction of their lesions by decompression from below. There was one death in this series (Case 2), a 94-year-old woman who died of pulmonary embolism forty-eight hours after her volvulus had been satisfactorily reduced. One patient (Case 6) represented a volvulus complicating a megacolon, a feature of the latter disease that has been commented on by others.[21-23]

This conservative method of treatment represents a rational attack on acute sigmoid volvulus, but before attempting it in the individual patient certain criteria must be satisfied:

1. *The diagnosis must be accurate* for obviously this method is of little value in the treatment of other forms of large bowel obstruction.

The previous history of patients with volvulus of the sigmoid is usually characterized by chronic or periodic constipation. Flatulence is also a prominent symptom and there have frequently been mild attacks of abdominal pain suggesting that incomplete volvulus has occurred and corrected itself a number of times prior to the major bout which brings the patient to the hospital.

The severity of the presenting symptoms and the speed with which they develop is naturally dependent upon the degree of rotation, the completeness of occlusion of the lumen, and the degree of disturbance of the bowel circulation. *Pain* is an early and prominent symptom. It is usually fairly continuous, due to traction on the mesentery, with colicky exacerbation due to hyperperistalsis. It is generally localized to the umbilical region or to the left lower quadrant. As peritonitis develops the pain may become more diffuse. *Constipation* is the rule but an occasional patient will complain of diarrhea, with the passage of blood or bloody mucus. *Vomiting* is not as common a symptom as in other forms of obstruction but eructations are noted fairly frequently.

Extreme distension of the abdomen is the characteristic and typical finding. If the abdominal wall is relaxed it may be possible to trace the ballooned sigmoid loop as it rises from the pelvis and extends high into the abdomen. Percussion over this distended loop gives a variable note depending upon the amount of fluid and gas it contains. Hyperperistalsis is present unless strangulation or peritonitis occurs. There may be marked tenderness over the loop if the circulation is compromised.

The x-ray picture of volvulus of the sigmoid colon is characteristic.[22, 24, 25] (See Fig. 1.) A flat plate of the abdomen reveals tremendous distension of the sigmoid flexure which pushes well out of the pelvis, almost always to the right side, often up to the diaphragm. A tremendous accumulation of fluid in the closed loop can be seen in the upright position. It is often possible to see two points of obstruction at the sites at which the bowel is twisted.[22] This latter is never seen with obstruction due to carcinoma of the colon, except in the rare case of two coexisting lesions. In volvulus, too, the two parts of the distended coil usually show uniform expansion, while in carcinomatous obstruction, the right half is more distended because the cecum and ascending colon are more distensible.[24, 25]

Barium enema examination usually demonstrates a spiral narrowing at the site of obstruction that has been variably described as "bird's bill,"[20] "snake's head,"[24] or "ace of spades"[5] deformity.

2. *The bowel circulation must be intact.* A silent abdomen, marked abdominal tenderness, fever and leukocytosis should all be indications for *operative* intervention. When in doubt as to the adequacy of the circulation, operate! Nonoperative reduction of an already strangulated loop of bowel does not restore viability.

3. *The torsion must be adequately reduced.* Although enemas have occasionally been successful in reducing the volvulus,[13, 20] the effect is often uncertain and temporary.

The best method of decompression from below is that described by Bruusgaard.[20] A proctoscope is inserted as far as the site of torsion with the aid of

careful inflation of the rectum. The site is easly recognized by the spiral folds seen there. Proctoscopic examination provides the examiner with an impression of the condition of the bowel, the appearance of the mucous membrane, and the blood supply at the site of the torsion. In some cases the appearance of the mucous membranes may be such that the examiner considers it dangerous to insert the tube. When the site of torsion has been located a well-lubricated, soft-rubber rectal tube, 60 cm. long and about the thickness of a finger, is guided up past the site of obstruction. Force must not be used, but the tube usually slips into place without trouble. There is very seldom doubt whether the treatment has succeeded because a forceful evacuation of flatus and thin stool is immediate, and the patient feels instant relief. The result may be verified by x-ray examination. In those cases where attempted intubation is unsuccessful, immediate laporatomy is indicated.

4. *The reduction must be maintained.* Recurrence has been known to occur within a few hours after reduction.[20] Therefore, it is necessary that the tube remain in place two or three days after reduction and should be sewn or securely strapped to the anus. The patient should be observed very closely the first few days after treatment. Frequent irrigation of the rectal tube may be necessary as it becomes plugged with feces.

5. *Recurrence should be prevented.* With a known incidence of recurrence of 20 to 30 per cent,[5-7, 9] it would perhaps be wise to prepare the patient for primary resection of the redundant loop of sigmoid colon while he is still in the hospital unless, of course, there are specific contraindications to surgery. Wangensteen[20] has reported two cases treated by elective resection two weeks following successful reduction by proctoscopic intubation, both with excellent results.

Some surgeons warn against the method just described because of the danger of perforation or the presence of unrecognized gangrene of the bowel. Bruusgaard's[20] work is adequate refutation of this thesis. Perforation of the bowel occurred only once in 168 trials. He was successful in reducing the volvulus in 123 cases, unsuccessful in 9. In the latter, immediate laparotomy was performed and the unsuccessful attempt shown to have no apparent untoward effect on the bowel. Four other cases died in spite of successful reduction, not because of the treatment (as did our Case 2). The volvulus had been completely reduced and the circulation was intact at post-mortem examination in each case.

If the technique of proctoscopic intubation and the criteria for its use herein presented are carefully followed, we believe it a safe and logical method of treatment for the acute attack of sigmoid volvulus.

SUMMARY AND CONCLUSIONS

The comparative experience of American and Scandinavian surgeons with acute volvulus of the sigmoid colon is discussed. Seven cases of this condition relieved by decompression from below are presented. The technique of proctoscopic intubation of the obstructed loop of bowel is described and the criteria for its proper use enumerated. We believe that where strangulation of the

bowel can be ruled out, the treatment of choice in sigmoid volvulus is proctoscopic intubation of the twisted loop, followed in ten days to two weeks by elective primary resection of the redundant sigmoid colon.

REFERENCES

1. Leonard, E. D., and Derow, J.: Volvulus, A Study of 22 Cases, New England J. Med. **218**: 388, 1938.
2. McIver, M. A.: Acute Intestinal Obstruction: Acute Mechanical Obstruction Exclusive of Those Due to Neoplasms and Strangulated External Hernias, Arch. Surg. **25**: 1106, 1932.
3. Keefe, John W.: Volvulus of the Large and Small Intestine, With Report of a Case of Volvulus of the Cecum, Ascending Colon and Ileum, Am. J. Surg. **17**: 345-348, 1932.
4. Michel, M. L., and McCafferty, E. L., Jr.: Volvulus of the Colon. A Study of Twenty-four Cases, South. Surgeon **14**: 525, 1948.
5. Griffin, W. D., Bartron, G. R., and Meyer, K. A.: Volvulus of the Sigmoid Colon. Report of 25 Cases, Surg., Gynec. & Obst. **81**: 287, 1945.
6. Bloodgood, J. C.: Intestinal Obstruction Due to Volvulus or Adhesions of the Sigmoid Colon, With a Report of Five Cases, and a Study of Etiological Factors, Ann. Surg. **49**: 161, 1909.
7. McKechnie, R. E., and Priestley, J. T.: Volvulus of the Small Intestine, Am. J. Surg. **34**: 286, 1936.
8. Rowlands, R. P.: Volvulus of the Intestine, Brit. M. J. **1**: 287, 1929.
9. Hinton, D., and Steiner, C. A.: Recurrent Volvulus of the Sigmoid Colon, Ann. Surg. **116**: 147-149, 1942.
10. Simon, H. E., Senturia, H. R., and Keller, T. B.: Volvulus of the Sigmoid Colon, Am. J. Surg. **71**: 550, 1946.
11. Finsterer, H.: Quoted by Baronofsky.[12]
12. Baronofsky, I. D.: Primary Resection and Aseptic End-to-End Anastomosis for Acute or Subacute Large Bowel Obstructions, SURGERY **27**: 664, 1950.
13. Metheny, D., and Nichols, H. E.: Volvulus of Sigmoid, Surg., Gynec. and Obst. **76**: 239, 1943.
14. Braun, W., and Wortmann, W.: Der Darmverschluss und die Sonstigen Wegstoerungen des Darmes, Berlin, 1924, J. Springer.
15. Perlmann, J. J.: Klinische Beiträge zur Pathologie und chirurgischen Behandlung des Darmverschlusses, Arch. f. klin. Chir. **137**: 245, 1925.
16. Faltin, R.: Einiges zur Kenntnis der Darmknoten, Acta. chir. Scandinav. **80**: 1, 1938.
17. Laurell, H.: Om Röntgen vid akuta Bukfall Uppsalla, 1931, Quoted by Nørgaard.[19]
18. Nørgaard, F., and Holmgren, B. S.: Reduction of Sigmoid Volvulus Under Roentgenologic Control, Acta radiol. **22**: 404, 1942.
19. Nørgaard, F.: Bloodless Reduction Under Roentgenologic Control of Acute Volvulus of the Sigmoid Flexure, Acta chir. Scandinav. **90**: 17, 1944.
20. Bruusgaard, C.: Volvulus of the Sigmoid Colon and Its Treatment, SURGERY **22**: 466, 1947.
21. Weeks, C.: Volvulus of a Sigmoid Megacolon, Ann. Surg. **94**: 1050, 1929.
22. Rigler, L. G., and Lipschultz, O.: Roentgenologic Findings in Acute Obstruction of the Colon (With Particular Reference to Acute Volvulus of the Sigmoid), Radiology **45**: 392, 1945.
23. Melamed, A.: Volvulus of Megacolon Reduced During Barium Enema Examination, Radiology **45**: 392, 1945.
24. Bellini, M. A.: Volvulus of the Sigmoid: A New Radiologic Sign, Radiology **53**: 268, 1949.
25. Levitin, J., and Weyrauch, H. B.: Acute Obstruction of the Colon: Differential Diagnosis Between Volvulus and Cancer of Sigmoid Colon by Preliminary Roentgenogram, Am. J. Roentgenol. **53**: 132, 1945.
26. Gerwig, W. H.: Volvulus of the Colon, Arch. Surg. **60**: 721, 1950.

CARCINOMA OF THE THYROID AND NONTOXIC NODULAR GOITER

ELMO J. CERISE, M.D.,* SPEARS RANDALL, M.D.,** AND
ALTON OCHSNER, M.D.,*** NEW ORLEANS, LA.

INTRODUCTION

BECAUSE clinical differentiation between benign and malignant nodules in the thyroid is frequently impossible, and because many cases of carcinoma of the thyroid develop in pre-existing adenomas, most physicians are now recommending surgical removal of all nodules from the thyroid. Members of the surgical department in this Clinic, like others,[1-3] have long believed that it is frequently impossible to differentiate, clinically, early carcinoma from adenoma of the thyroid, that carcinoma is often present in a gland with multiple nodules, and that unless definitely contraindicated, *all* nodular goiters should be removed. However, there are some who believe that carcinoma in the thyroid is uncommon[4, 5] or that it usually can be diagnosed clinically.[6] In an attempt to settle this difference of opinion a study of the comparison of the results of surgical treatment with those of conservative treatment of nodular goiters was undertaken.

MATERIAL

During a period of 7 years ending in April, 1949, 51 histologically proved cases of carcinoma of the thyroid and 529 cases of nontoxic nodular goiter were encountered at the Ochsner Clinic. Forty-seven of the 51 patients with carcinoma were followed for periods up to 7 years. Most of the patients were referred, but in 6 the disease was discovered on routine examination. Most of the patients were from a nongoitrous region.

ANALYSIS OF CASES

Incidence.—Of the 580 cases of nodular goiter, there were 51 cases of carcinoma, or an incidence of 8.8 per cent, which is similar to the incidence in other reported series (Tables I and II). However, 8 of the 51 patients with carcinoma had been operated on previously, so that the contour of the gland could not be determined by us. Therefore, of the remaining 572 patients with nodular thyroid, 387 had single nodules. Of these latter 30, or 7.7 per cent, were malignant. Of the 185 cases of multiple nodular goiter 13, or 7 per cent, were malignant.

More important, and probably more accurate, however, is the incidence of carcinoma of the thyroid found in nodular thyroid glands at operation. In the

Received for publication, Aug. 8, 1951.

*Fellow in Surgery, Alton Ochsner Medical Foundation.
**Departments of Pathology, Tulane University of Louisiana, School of Medicine and Ochsner Clinic.
***Departments of Surgery, Tulane University of Louisiana, School of Medicine and Ochsner Clinic.

present series, 121 patients with single nontoxic nodular goiters and 30 with carcinoma in solitary nodular glands were operated upon, making a total of 151 cases of solitary nodular thyroid in which operation was done. The operative incidence of carcinoma of the thyroid in solitary nodules was thus 19.8 per cent. There were 88 patients with multiple nontoxic nodular goiter and 13 with carcinoma in multiple nodular glands operated upon, making a total of 101 patients with multiple nodular glands operated upon. Therefore, the operative incidence of carcinoma in thyroids containing multiple nodules was 12.8 per cent. Tables III and IV show a comparison of the incidence of carcinoma in single and multiple nontoxic goiter between the present series and that reported by others. It should be pointed out that a gland was considered to contain multiple

TABLE I. INCIDENCE OF CARCINOMA IN NONTOXIC NODULAR GOITER

	NODULAR GOITER	CARCINOMA	
	CASES	CASES	PER CENT
Hare[7]	5,052	246	4.8
Ward[3]	3,539	168	4.8
Hinton and Lord[8]	184	14	7.6
Anglem and Bradford[9]	550	42	7.6
Cole et al.[2]	192	33	17.1
Crile[6]	274	20	10.9
Ochsner Clinic	580	51	8.8
Operated	210	43	17.3

TABLE II. INCIDENCE OF CARCINOMA IN GOITER (PERLOFF AND SCHNEEBERG[10])

	GOITER	CARCINOMA	
	CASES	CASES	PER CENT
Nodular goiter (toxic and nontoxic)	345	18	5.2
Smooth goiter	545	16	2.9
Total thyroid (collected cases)	59,603	1,671	2.8
Nodular (collected cases)	7,149	367	5.1

TABLE III. INCIDENCE OF CARCINOMA IN SINGLE NONTOXIC NODULAR GOITER

	OPERATED CASES OF SOLITARY NODULAR GOITER	CARCINOMA	
		CASES	PER CENT
Anglem and Bradford[9]	363	33	9.0
Hare[7]	1,971	236	12.0
Cole et al.[2]	92	22	24.0
Crile[6]	98	24	24 5
Ochsner Clinic	151	30	19.8

TABLE IV. INCIDENCE OF CARCINOMA IN MULTIPLE NONTOXIC NODULAR GOITER

	OPERATED CASES OF MULTIPLE NODULAR GOITER	CARCINOMA	
		CASES	PER CENT
Anglem and Bradford[9]	187	9	4.8
Cole et al.[2]	100	11	11.0
Crile[6]	176	6	3.4
Ochsner Clinic	101	13	12.8

nodules if the nodules appeared multiple to the operator even though microscopically they were not true multiple adenomas but perhaps colloid nodular areas.

Sex.—In this series there were 438 women and 91 men with nontoxic nodular goiters, or a ratio of 5 women to 1 man. There were 38 women and 13 men with carcinoma of the thyroid, or a ratio of 3 to 1. These figures, which are similar to those reported by others, again show that although carcinoma of the thyroid occurs more often in women, it is relatively more frequent in men than is benign nontoxic nodular goiter.

Age.—The average age in the 51 cases of carcinoma was 47 years, with a range of from 12 to 83 years. Five patients were 30 years of age, or younger. We agree with Lahey[1] that it is particularly important to remove nodules from the thyroids of these young people because of the possibility of malignancy.

Duration of Nodule.—In this series there were 46 cases of carcinoma of the thyroid in which a mass (thyroid gland, enlarged nodes, or both) was palpable in the neck, and the duration of the mass was recorded. In many of these, this was, of course, approximated by the patient. The average duration was 5.7 years with a range of 0 days (discovered on routine examination in 6 cases) to 30 years. Eleven patients had had a known thyroid nodule more than 10 years.

In 38 cases of carcinoma, an effort was made to determine the interval between the initial examination for the condition and admission to the Clinic for treatment. The average interval in these cases was 2.8 years; 8 patients did not have definitive treatment until more than 5 years after they were told that the thyroid was abnormal.

These figures, we believe, bring out several important points. In the first place, many of the nodules, having been present for a long time (average 5.7 years), were probably benign adenomas originally. It has been reported that about 80 per cent of carcinomas of the thyroid arise from pre-existing adenomas. It is impossible to determine this with complete accuracy by histologic means, because the carcinoma often completely replaces the benign tumor; however, even taking into consideration that some carcinomas of the thyroid are slow growing. the long average duration of these tumors would make one think that many were originally benign. In our series some of the patients with the most malignant tumors admitted having had thyroid enlargement as long as 13 and 25 years previously. This differs from the observation of Crile,[11] who in his last study reported that 80 per cent of highly malignant tumors arose suddenly with no history of previously recognized benign goiter. Although the patients with carcinoma of low-grade malignancy in his series had noted a thyroid nodule for an average of 5 years previously, he assumed that the malignancy was low grade from the beginning.

In the second place, whereas many of these patients were undoubtedly advised to have an operation sooner but had procrastinated, there were also many who were told the nodule was "not serious." Of course, some patients were probably examined by physicians who, although cognizant of the danger of carcinoma, believed they could differentiate it from benign nodular goiter clinically. As will be pointed out later, this, too, is a mistake.

Thus, these patients would have been treated (in many cases prophylactically) on an average of 5.7 years sooner if they had been properly informed, and treatment should have been undertaken at least 2.8 years sooner in those patients in whom the malignant condition was recognized.

Clinical Manifestations.—The commonest manifestation in this series was the presence of a mass in the neck (either thyroid or nodes), noted in 44 patients. Other complaints were hoarseness in 7 patients, vocal cord paralysis in 6, dyspnea in 7, and a pressure sensation in 6. Only 6 patients noted rapid increase in size of the nodule and 6 complained of gradual increase in size. No patient was considered definitely toxic. Four patients had no symptoms, the disease being discovered on routine examination. Several patients had evidences of advanced disease, such as loss of weight, anorexia, and pain. Thus, if one waits for the usual signs of malignancy of the thyroid, such as fixation of the gland and rapid increase in size, many of the early lesions will be overlooked.

It is interesting to note that 4 patients with benign adenoma had paralysis of the vocal cord prior to operation, and in 2 of these, complete function was restored after removal of the adenoma.

In *all* of our cases a laryngoscopic examination was performed both preoperatively and postoperatively. This is a routine procedure here for all patients scheduled for thyroid surgery. According to Laszlo[12] about 10 per cent of all patients with thyroid disease have paralysis of one vocal cord preoperatively without the patient or surgeon knowing about it. Unilateral paralysis of cords may cause only slight hoarseness, which could be easily overlooked unless the vocal cord is routinely examined postoperatively.

Diagnosis.—Crile[6] reported a definite preoperative diagnosis of malignancy in 27 of 30 cases of carcinoma of the thyroid and a suspected diagnosis in 2 others. In other words, he was able to make a correct diagnosis preoperatively in 97 per cent of cases. Although he admitted that this figure is abnormally high, he believed that a diagnostic accuracy of 90 per cent is possible.

Rogers, Asper, and Williams[5] reported 64 cases in which the correct diagnosis was made or highly suspected in 48 per cent preoperatively. In Cole's[13] cases, only 21 per cent were diagnosed preoperatively, 21 per cent at operation, and the remainder microscopically. Thus, 80 per cent of his cases were not diagnosed clinically, and 60 per cent were overlooked surgically.

In our own series there were 10 cases in which a positive histologic diagnosis was made before the patient came to us. Of the remaining 41 cases, the condition was highly suspected in 3 cases and definitely recognized preoperatively in 12 cases; in other words, the diagnostic accuracy in our series was 36.6 per cent. Ten cases, or 24.4 per cent, were recognized at operation and 16 cases, or 39 per cent, in the laboratory.

Ward[3] found a five-year survival in only 20 per cent of those diagnosed preoperatively, in 40 per cent of those diagnosed at operation, and in 80 per cent of those cases diagnosed histologically. Among our own cases, there were 11 patients with carcinoma, not diagnosed previous to admission, who are known to be dead. In 8 of these 11 cases the diagnosis was made or highly suspected

preoperatively. Ten cases were diagnosed at operation and 3 of these could not be followed. However, the remaining 7 have no evidence of recurrence. Of 16 cases diagnosed in the laboratory, 3 are known to be dead, one has a probable recurrence, and one could not be followed. The remaining 11 are well. Thus, of the 26 cases, 18 are well, 4 could not be followed, 3 are dead, and one has a probable recurrence.

This, we believe, again shows that early carcinoma cannot be differentiated from benign adenoma in many cases, and if the longest possible survival is to be achieved, one cannot wait for the positive signs of malignant disease before advising operation.

Type of Operation.—In this series, 49 patients were operated upon by us. The types of operations are shown in Table V. Obviously, at times, some of the major procedures were combined; for example, total or subtotal thyroidectomy was combined with radical neck dissection. In all, there were 49 major procedures, which include the cases of total and subtotal thyroidectomy, decompression, and radical neck dissection.

TABLE V. OPERATIVE PROCEDURES ON 49 PATIENTS WITH CARCINOMA OF THYROID

	CASES
Hemithyroidectomy (subtotal resection)	36
Total thyroidectomy	8
Radical neck dissection	14
Decompression (only part of tumor removed)	6
Tracheotomy	9
Lymph node biopsy	13

Of the 529 patients with nontoxic nodular goiter, 210 or 39 per cent underwent subtotal thyroidectomy. In 49 patients, or 9 per cent, there was a definite contraindication to operation. In the remaining cases operation was advised but was either refused or postponed.

Operative Mortality.—Following the 49 major operative procedures for carcinoma, there were 5 deaths, or a mortality rate of 10.2 per cent. In the 210 operations for nontoxic nodular goiter, there were no operative deaths, but one patient died during induction of anesthesia, before the actual operation was begun.

Other Therapy.—Of the 51 patients with thyroid carcinoma, 34, or 66 per cent, received roentgen-ray therapy postoperatively. There is some disagreement as to whether roentgen-ray therapy should be employed postoperatively. Hare and Swinton[14] apparently favored its routine use, whereas Portmann[15] believed that all patients should receive roentgen-ray treatment except those with malignant adenomas or papillary carcinomas which are small, well confined to the thyroid tissue removed, and discovered only on pathologic examination. This has generally been our policy. As Haagensen[16] reported in 1931, "the less rapidly growing and less anaplastic thyroid tumors are moderately radiosensitive, while the rapidly and highly anaplastic types are not affected by radiation." It is generally agreed that papillary carcinoma of the thyroid is most radiosensitive, but benefit may be obtained in other types.

Six patients, or 10 per cent of the series, received radioactive iodine. Our experience has been the same as that of others, in that the amount of uptake by the individual tumors varies a good deal and makes its benefit somewhat limited.

Pathology.—Microscopic examination of tissue was performed in all 51 cases with thyroid carcinoma. Our classification in 44 cases is shown in Table VI. In the 7 cases in which histologic material was not available to us for review, the diagnosis submitted by the referring pathologist has been given (Table VI).

TABLE VI. CLASSIFICATION OF 51 CASES OF THYROID CARCINOMA

		CASES	PER CENT
Predominantly papillary adenocarcinoma		12	27.2
Mixed papillary adenocarcinoma		13	29.5
Follicular and alveolar adenocarcinoma component	11		
Solid adenocarcinoma component	1		
Hürthle-cell carcinoma component	1		
Follicular and alveolar adenocarcinoma		7	15.9
Solid adenocarcinoma		7	15.9
Hürthle-cell carcinoma		3	6.8
Spindle- and giant-cell carcinoma		2	4.5
Classified elsewhere as		7	
Papillary adenocarcinoma	3		
Adenocarcinoma	4		

Although there are various classifications of thyroid carcinoma, we have adopted that employed at Memorial Hospital, New York City, because of its relative simplicity and general adaptability. We have not attempted to grade thyroid carcinoma by the method followed in other types of cancer because the clinical course is too unpredictable. It seems to us that more would be gained from a clinical standpoint by accepting and understanding a working classification of thyroid cancer based on types rather than "grade."

On the basis of five-year survival, Frazell and Foote[17] studied 215 patients out of a series of 301 cases of thyroid cancer. In this group the five-year survival rates were as follows: papillary adenocarcinoma, 79 per cent; follicular and alveolar adenocarcinoma, 28.6 per cent; solid adenocarcinoma, 23 per cent; Hürthle-cell carcinoma 33.3 per cent; and giant- and spindle-cell carcinoma 0 per cent. Our own series shows this same trend of survival.

We are in agreement with those[11, 18] who believe that the "lateral aberrant thyroid" represents metastasis from a primary carcinoma of the thyroid. Warren and Feldman[18] reported 49 cases of lateral aberrant thyroids in which a primary tumor was found in the thyroid gland. In the 8 patients in whom the tumor was not found, the thyroid was not removed; in 4 of the cases, the gland was thought to be negative to palpation at operation.

In the present series, there were 12 cases in which only a node or nodes were palpable in the neck, and on removal were found to be "lateral aberrant thyroid." In 9 of these cases, the primary tumor was proved to be in the homolateral lobe of the thyroid when removed later. Exploration was not done in the other 3 cases.

TABLE VII. METASTASIS IN 51 CASES OF CARCINOMA OF THYROID

	CASES
Cervical lymph nodes	21
Trachea	8
Muscles of neck	8
Esophagus	3
Pharynx	1
Larynx (cord paralysis)	6
Distant (lungs, bones, liver)	6

Thus, in every case of "lateral aberrant thyroid" in which the homolateral lobe of the thyroid was removed, the primary tumor was found in the gland. In each instance, the primary tumor resembled the metastases histologically.

Follow-up Study.—Of the 51 patients with carcinoma, 47, or 92 per cent, could be followed for periods ranging from 1.5 to 7 years. Since carcinoma of the thyroid frequently recurs after many years of an apparent "cure," a prolonged follow-up is especially important. In this series, the follow-up is admittedly too short to permit final conclusions. Eight, or 17 per cent, are already known to be dead from the neoplasm, whereas 5 are dead from other causes. Of the remaining 34 patients followed, 17 did not have metastases when seen originally and these are all perfectly well. In the other 17 cases, 3 have proved recurrence, and 2 others are thought to have a recurrence, thus leaving 12 more believed to be well (Table VIII).

TABLE VIII. FOLLOW-UP IN 47 CASES OF CARCINOMA OF THYROID

	CASES	PER CENT
Dead		
From disease	8	17.0
From other causes	5	10.6
Probable recurrence	5	10.6
Apparently well	29	61.8
Total	47	100.0

An attempt was made to follow those 529 patients with nodular goiter, in the hope of determining the number of people with clinically nodular nontoxic goiter who refused surgical treatment and in whom carcinoma eventually developed, and also the number of cases of nodular goiter in which removal was followed by recurrence of an adenoma, or the development of a malignancy. It is, however, regrettable that only about 50 per cent could be followed. There were no known patients in whom carcinoma later developed, but the number for whom follow-up responses were obtained is insufficient for definite conclusions.

DISCUSSION OF TREATMENT

Our experience with carcinoma of the thyroid has convinced us that we are unable to differentiate it clinically from benign nodular goiter in at least half the cases. This is true in spite of being "cancer conscious" and sufficiently impressed with its frequency to recommend prophylactic thyroidectomy for nodular goiters. We wish that it were possible to diagnose carcinoma of the

thyroid *early* by clinical means, but until such a time as it becomes possible, we must continue to treat it with our best available weapon—prophylactic thyroidectomy.

After the physician has become convinced that thyroidectomy is the treatment of choice for *all* nodular goiters, it then becomes the responsibility of the surgeon to make this operation as safe as possible. The number of early carcinomas overlooked, in addition to the greater number of complications following operation for carcinomas, makes "watching" a nodular goiter unjustifiable. The only way we can decrease the mortality and complications in thyroid carcinoma is by early removal. Early removal is possible in all but the few rapidly growing malignancies of the thyroid, and if this were done, the complications following operation for carcinoma would be nearly the same as for benign goiter.

In removing a clinically benign goiter, we agree with Ward[19] that normal thyroid tissue around the capsule of the nodule should be removed. Just as tumors of the breast should not be enucleated, we believe that this should not be done in the thyroid.

It is also the policy in our Clinic to obtain a frozen section of all nodular goiters removed. This is important, in view of the fact that 46 per cent of our cases were not diagnosed until examined microscopically.

Once the diagnosis of malignancy of the thyroid has been confirmed, there is still controversy as to the treatment of choice. If the malignancy is apparently confined within the gland, and no nodes are palpable on exploration of the neck, some believe that hemithyroidectomy with removal of the isthmus is sufficient. Others prefer the more radical operation of Crile and Crile,[20] in which the internal jugular vein on the involved side is resected, so as to include the superior and middle thyroid veins, and the inferior thyroid vein is ligated low, in addition to total removal of the involved lobe without bothering to expose the recurrent laryngeal nerve, and without applying instruments or sutures to the lobe. The principle on which this procedure is based is that carcinoma spreads first by venous channels, and by the lymphatics only after the capsule has been invaded.

The opinions among the members of our surgical department vary as to the best method of treatment, with considerable individualization of treatment with each patient. It is well to note that during the period of this study, the 9 patients in whom radical neck dissections were performed for carcinoma of the thyroid all had known extension of the tumor into the cervical lymph nodes or soft tissues of the neck. Since this study, however, there have been some radical neck dissections for thyroid carcinoma without local metastases. The operation of Crile and Crile is seldom performed here for this type of case, but instead hemithyroidectomy with removal of the isthmus is done.

We believe that those patients with thyroid carcinomas which have spread to involve local structures—such as strap muscles, or the recurrent laryngeal nerve—or in which the cervical nodes are enlarged, should all have radical neck dissection and hemithyroidectomy with removal of the isthmus. Since we believe

that the "lateral aberrant thyroid" represents metastasis to a cervical node, these patients are treated by radical neck dissection along with hemithyroidectomy.

In those patients with thyroid carcinoma in which the tumor has infiltrated to such an extent that complete local resection is impossible, we believe, as does Cattell,[21] that in addition to decompressing the trachea, as much of the tumor as possible should be removed. These patients frequently require tracheotomy also, at least during the period of postoperative roentgentherapy. If a great deal of the tumor is removed, and roentgentherapy is given postoperatively, these patients frequently live longer and more comfortably than one would expect.

Local recurrences, or recurrences in cervical lymph nodes, we believe, should be treated by radical neck dissection, and apparently not as does Crile,[22] only by excision of the nodes. Radical block dissection should always include removal of the sternocleidomastoid and pretracheal muscles, resection of the cervical nodes, internal jugular vein, and homologous thyroid lobe.

Most of our patients with thyroid carcinoma received either postoperative roentgentherapy, or radioactive iodine. The papillary carcinomas are the most radiosensitive,[23] but benefit may be obtained from irradiation in the other types. We are continuing to use radioactive iodine in those cases in which it is applicable, but the results thus far are not conclusive.

SUMMARY

An analysis of 51 proved cases of carcinoma of the thyroid compared with 529 cases of nontoxic nodular goiter seen over a period of 7 years is presented. The incidence of carcinoma discovered at operation was 19.8 per cent in glands with single nodules, and 12.8 per cent in glands with multiple nodules. In the cases of carcinoma, the average interval between discovery of the tumor and institution of definitive treatment was 5.7 years and between the discovery of the tumor and the time the thyroid was first examined by a physician it was 2.8 years. The diagnosis of carcinoma was not recognized clinically in 63.4 per cent of the cases and was not made at operation in 39 per cent of the cases. In the 9 cases of "lateral aberrant thyroid" in which the homolateral lobe of the thyroid was removed, the primary carcinoma was found in the lobe in each instance. The admittedly short term follow-up revealed that about 60 per cent of the patients in the present series are apparently well, and about 17 per cent are dead as a result of the neoplasm.

The surgical treatment for carcinoma of the thyroid at the Clinic is individualized to suit the case. In general it can be said that hemithyroidectomy with removal of the isthmus is performed on patients whose tumor is limited to the thyroid gland. If the lesion has spread to the cervical nodes, or locally to muscles, or if there is evidence of local recurrence, radical neck dissection is performed. Patients with massive involvement are best treated by removal of as much tissue as possible, decompression of the trachea, tracheotomy and postoperative roentgentherapy.

CONCLUSIONS

1. We are unable to diagnose carcinoma of the thyroid early by present clinical means.

2. The incidence of carcinoma in both single and multiple nodular goiters is sufficiently high to warrant prophylactic thyroidectomy for *all* nodular goiters unless a definite surgical contraindication exists.

3. "Lateral aberrant thyroids" are in reality metastases in cervical lymph nodes and should be so treated.

REFERENCES

1. Lahey, F. H.: Carcinoma of the Thyroid, Am. J. Roentgenol. **46**: 469-475, 1941.
2. Cole, Warren, Slaughter, D. P., and Rossiter, L. J.: Potential Dangers of Nontoxic Nodular Goiter, J. A. M. A. **127**: 883-888, 1945.
3. Ward, Robertson: Malignant Goiter, SURGERY **16**: 783-803, 1944.
4. Vanderlaan, W. P.: The Occurrence of Carcinoma of the Thyroid in Autopsy Material, New England J. Med. **237**: 221-222, 1947.
5. Rogers, W. F., Jr., Asper, S. D., Jr., and Williams, R. H.: Clinical Significance of Malignant Neoplasms of the Thyroid Gland, New England J. Med. **237**: 569-576, 1947.
6. Crile, George, Jr.: Practical Aspects of Thyroid Disease, Philadelphia, 1949, W. B. Saunders Company.
7. Hare, H. F.: Cancer of the Thyroid, S. Clin. North America **27**: 561-568, 1947.
8. Hinton, J. W., and Lord, J. W., Jr.: Is Surgery Indicated in All Cases of Nodular Goiter, Toxic and Nontoxic? J. A. M. A. **129**: 605-606, 1945.
9. Anglem, T. J., and Bradford, M. L.: Nodular Goiter and Thyroid Cancer, New England J. Med. **239**: 217-220, 1948.
10. Perloff, W. H., and Schneeberg, N. G.: The Problem of Thyroid Carcinoma, SURGERY **29**: 572-580, 1951.
11. Crile, George, Jr.: Factors Influencing the Prevention and Cure of Cancer of the Thyroid, Surg., Gynec. & Obst. **91**: 210-214, 1950.
12. Laszlo, A. F.: Laryngeal Complications After Thyroid Operation; Symptoms, Prognosis and Treatment, Am. J. Surg. **73**: 62-68, 1947.
13. Cole, W.: Quoted by Powell, R. A.: Carcinoma of the Thyroid and Nodular Goiter at the Blain Clinic, Alex. Blain Hosp. Bull. **9**: 111-119, 1950.
14. Hare, H. F., and Swinton, N. W.: Cancer of Thyroid, J. A. M. A. **110**: 327-329, 1938.
15. Portmann, U. V.: Malignant Tumors of the Thyroid Gland, Surg., Gynec. & Obst. **70**: 185-192, 1940.
16. Haagensen, C. D.: Cancer of the Thyroid: Its Radiosensitivity, Am. J. Cancer **15**: 2063-2105, 1931.
17. Frazell, E. L., and Foote, F. W., Jr.: The Natural History of Thyroid Cancer, J. Clin. Endocrinol. **9**: 1023-1030, 1949.
18. Warren, Shields, and Feldman, J. D.: The Nature of Lateral Aberrant Thyroid Tumors, Surg., Gynec. & Obst. **88**: 31-44, 1949.
19. Ward, Robertson: Malignant Disease of the Thyroid Gland, J. Internat. Coll. Surgeons **10**: 404-407, 1947.
20. Crile, George, and Crile, George, Jr.: A Radical Operation for Malignant Tumors of the Thyorid Gland, Surg., Gynec. & Obst. **64**: 927-934, 1937.
21. Cattell, R. B.: A More Optimistic Approach to Carcinoma of the Thyroid, West. J. Surg. **54**: 444-449, 1946.
22. Crile, George, Jr.: Disease of the Thyroid, Postgrad. Med. **1**: 51-57, 1947.
23. Horn, R. C., Welty, R. F., Brooks, F. P., Rhoads, J. E., and Pendergrass, E. P.: Carcinoma of the Thyroid, Ann. Surg. **126**: 140-155, 1947.

A SUGGESTED TERMINOLOGY FOR LIGAMENTS OF THE GROIN; THEIR CLINICAL AND SURGICAL APPLICATION IN REPAIR OF HERNIAS

CLAUD C. BURTON, M.D., DAYTON, OHIO

(From the Veterans Administration Center, Dayton, Ohio, and the Department of Surgery, University of Cincinnati College of Medicine)

ANATOMY of the inguinal region is as old as our knowledge of human anatomy, yet, as surgeons, we are steadily learning more about the function and practical surgical relationship of these anatomic structures. The varied interpretation of this relationship forms the basis for the innumerable technical maneuvers that have been proposed for repair of hernias of this region. As a result of the advancement in the practical application of anatomic knowledge, it has become necessary to revise certain previously accepted orthodox concepts of anatomy, just as it has been essential in many instances to progressively modify certain details of recognized technical procedure.

Since the anatomist or surgeon, each through his enthusiasm stemming from a new anatomic discovery or from the introduction of a new technique, stresses the importance of his particular field of endeavor, there may unconsciously develop an imbalance in our correlative anatomic and surgical knowledge. Perhaps this is the penalty of too rapid progression before reaching standardization, but any divergence of opinion that might obtain in the integration of the allied sciences and anatomy and their practical application should not be long lasting. It is therefore inevitable that, at periodic intervals, it becomes necessary to assay anatomic and surgical views so that they will mesh clinically and therapeutically. For instance, a recent medical graduate can quickly enumerate the various coverings of different types of hernias and describe classical technical reparative procedures more completely and exactingly than many senior surgeons. This seemingly paradoxical lack of meticulous anatomic knowledge of the latter is traceable to the fact that too often anatomic evaluations are at variance with their clinical and surgical importance. To illustrate, one need only refer to the little available information in most textbooks of anatomy on Cooper's ligament,[17] yet it is of pivotal importance surgically in dealing with difficult hernias. In contrast, it has been the experience of surgeons that certain ostensibly important anatomic structures are of equivocal importance surgically, or cannot be demonstrated at the operating table.

The object of this paper is to analyze the eight intrinsic ligaments and one extrinsic ligament of the groin and to place them in their proper perspective in relation to the modern concept of hernia repair. This will entail reconcilia-

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Received for publication, June 22, 1951.

tion of varying terminology and synonyms which have been cumulative for three-quarters of a century. The success of this undertaking is somewhat dependent upon the sympathetic attitude of the reader; it is not likely to fare well if the reader approaches it dogmatically.

LIGAMENTS OF THE INGUINAL REGION

The ligaments of the groin may be divided into: (a) those that are essential to the integrity of the wall, and which, if they become attenuated or fragmented, or if there is evidence of aplasia, must be reinforced or replaced in order to attain a secure wall, and (b) those that are demonstrable anatomically, but of equivocal importance clinically or surgically, yet are perpetuated in the archives, chiefly because of their former embryological role, the pre-existing erroneous concept of their reparative value, or their significance as anatomic landmarks, such as boundaries of triangles or fossae.

Another, and what seems to us a more practical, classification of the ligaments of this region is proposed; according to their location and functional relationship. Consonant with this view, they have been divided into (1) longitudinal iliopubic ligaments, (2) auxiliary iliopubic ligaments, and (3) ligaments of the posterior wall of the canal. Desirable and rational as the latter classification may be, it does not seem advisable to be dogmatic and adhere to it undeviatingly. Since many concepts concerning the ligaments of this region are so deep rooted, any radical departure is almost certain to provoke acrimonious controversy unless some leeway is permitted. It is probable more progress can be made in our knowledge of these ligaments by a gradual evolution in our concept of them from their anatomical role to their clinical role as conceived and exemplified in the modern reparative techniques.

LONGITUDINAL ILIOPUBIC LIGAMENTS

There are three ligaments that logically fall in this category: (a) iliopubic anterior or inguinal, (b) iliopubic intermediate or iliopubic tract, and (c) iliopubic posterior or Cooper's ligament. These ligaments all arise from the ilium at varying levels and they all have a common insertion into, or adjacent to, the pubic spine. They all are used primarily for anchorage of the musculofascial wall; they run in the same general direction and are approximately the same length except Cooper's ligament, which is somewhat shorter. For the reasons enumerated, it would seem that they should be considered longitudinal ligaments. Such a designation would distinguish them from the auxiliary iliopubic ligaments and from ligaments of the floor of the canal.

Iliopubic Anterior Ligament (Inguinal Ligament or Poupart's Ligament).— This was the first ligament to be employed in hernia repair and it has retained a pre-eminent position in hernial surgery for three-quarters of a century. It continues to be the ligament most frequently used for anchorage of the parietal wall in reinforcing the floor of the inguinal canal. This is the only ligament of this region about which there is unanimous agreement as to anatomic origin and structural relationship. Since it is the continuation of the external apo-

neurosis, it is coincidentally subservient to any stress to which the wall is exposed or to any intra-abdominal force which may ultimately produce parietal weakness.

It is the longest, widest, and most easily accessible ligament of the groin, and the one about which there is least controversy. It is the dense, inferomedian component of the flat tendinous portion of the external oblique muscle, which stretches from the anterior superior iliac spine to the pubic spine. From it arise some of the fibers of the internal oblique and transversus abdominis muscles. Mediad the ligament may send some fibers to the pecten ossis pubis. It also projects inferiorly and attaches to the posterior iliopubic ligament forming the medial lacunar ligament which may be referred to as the pectineal portion of the anterior iliopubic ligament. Also, the lower margin of this ligament merges with the fascia lata. As a rule it is a strong and resistant ligament and because of its adjacent relationship to the parietal strata of the inguinal canal, it is the logical structure for attachment of the fascial boundary of the canal. It represents one of the earliest ligamentous structures used in reinforcing the weakness of the floor of the canal. In contrast, the ligament may possess certain objectionable features in that it may become attenuated, particularly in those individuals with mesenchymal deficiency, or those who are constantly subjected to increased intra-abdominal pressure. Moreover, in recurrent hernias the ligament is prone to fragmentation and fibroplasia from tension suture necrosis of previous repairs. In the event the ligament is found to be inadequate, it may require replacement with a pedicled fascial graft, reinforcement with an autogenous suture or, not infrequently, it may become necessary to substitute either the posterior iliopubic ligament or the intermediate iliopubic ligament. We prefer the former. Another frequently overlooked reparative feature of the anterior iliopubic ligament is the suturing of its turned down edge to the posterior iliopubic ligament which, in effect, bridges and reinforces the interligamentous space. This maneuver creates a strong surgical attachment to the posterior iliopubic ligament which exceeds in strength its anatomic origin.

The anterior iliopubic ligament is an important boundary of the surgical triangles of the inguinal region.[10] The pre-eminence of the anterior iliopubic ligament in hernia repair has been challenged only in the last two decades by its counterpart, the posterior iliopubic ligament, in cases of hernias presenting coexisting generalized mural weakness or interligamentous protrusions, and recurrent hernias for the repair of which the anterior iliopubic ligament is insufficient.

Iliopubic Intermediate Ligament (Iliopubic Tract).—Subjacent, parallel, and slightly posterior to the recurved edge of the anterior iliopubic ligament is a loosely attached, separable, dense band derived from the fascia transversalis. It extends from the anterior inferior spine of the ilium beneath the origin of the anterior iliopubic ligament to the common ligamentous conjunction at the pubic tubercle, blending with the posterior medial ligament of the canal, the aponeurosis of the transversus abdominis, and subjacently with the medial third of the posterior iliopubic ligament. It is considered a variant of the fascia transversalis and has been designated iliopubic tract by Quain[15] and by Clark

and Hashimoto.[8] According to these authors, the ligamentous tract is easily palpated as a constant, uniformly resistant structure which curves in front of the external iliac vessels where it is thicker due to reinforcement by an expansion of the psoas fascia. Inferiorly, it merges with the fascia of the pectineus and iliopectineal fascia. It lies in a laminar plane parallel with the abdominal inguinal ring and tendon of the transversus abdominis.

Clark and Hashimoto attribute much strength and stability to the intermediate iliopubic ligament and have employed it as anchorage for the medial

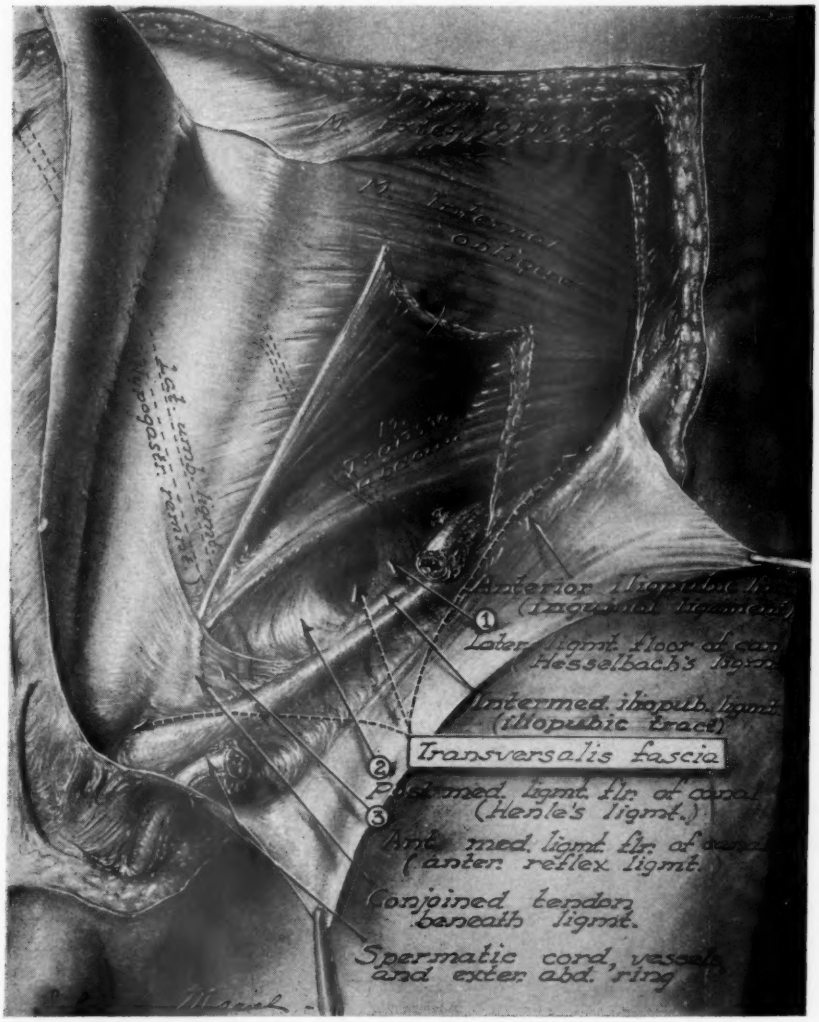


Fig. 1.—The anatomic structures of the left lower quadrant of the abdomen, anterior view. The external oblique muscle and its aponeurosis have been reflected, exposing the underlying internal oblique muscle. A triangular segment of the latter has been hinged by vertical section at the level of the abdominal ring. Reflecting this muscle mediad brings into relief the relationship of the transversus abdominis muscle. For the sake of a clear view of the floor of the canal, the spermatic cord has been sacrificed. The arrows identified by encircled numbers point to: (1) lateral ligament of the floor of the canal (Hesselbach's or interfoveolar ligament), (2) posterior medial ligament of the floor of the canal (Henle's ligament), and (3) medial anterior ligament of the floor of the canal (ligamentum inguinale reflexum), which are, for the most part, variants of the fascia transversalis. The lateral umbilical ligament and inferior epigastric vessels are shown. The fascia transversalis is indicated as continuing its internal laminar relationship with the parietal wall. In this view, only the anterior iliopubic ligament (inguinal ligament) and the posterior iliopubic ligament (Cooper's ligament) are illustrated.

fascial boundary of the floor of the canal by means of a triple interligamentous suture. The suture passes through the posterior medial ligament of the inguinal canal (Henle's ligament), posterior iliopubic ligament, and the intermediate iliopubic ligament. In their technique it is considered the first line of defense to intra-abdominal pressure. The wall, however, is further strengthened by suturing the inguinal falx medially, and more laterally the fibers of the internal oblique muscle which attach to the recurved portion of the anterior iliopubic ligament. The external oblique aponeurosis forms the third stratum of the wall in this technique.

Perhaps it would be apropos to consider some of the factors which may be raised and which contrive to make the intermediate iliopubic ligament a seldom used ligament in hernia repair: (1) the paucity of available or confirmatory information concerning this ligament, either in textbooks of anatomy or in the current literature, (2) the uncertainty of its identification at the operating table, (3) existing doubt as to its constancy, (4) lack of published statistical data by different surgeons who have employed this ligament, verifying its superiority over the standardized anterior iliopubic ligament repairs, and (5) the failure to establish criteria for its use.

My meager knowledge of the existence of the intermediate iliopubic ligament dates back to the publication of Clark and Hashimoto in 1946. I have tried, many times, after completing the dissection of the sac and cord, to identify this ligament which should be subjacent and parallel to the recurved component of the anterior iliopubic ligament; however, its presence can be verified only by reflecting the anterior iliopubic ligament, which obviously would be impracticable and unwise at operation. In the anatomic laboratory where more deliberate and meticulous dissection is possible, and where detachment of the anterior iliopubic ligament can be done with impunity, it can be demonstrated as a distinct entity. Therefore, for all practical purposes, the surgeon must consider the intermediate iliopubic ligament in much the same relationship to the anterior iliopubic ligament as that which exists between the medial lacunar ligament and the anterior iliopubic ligament.

Iliopubic Posterior Ligament (Cooper's Ligament, Iliopectineal or Pectineal Ligament).—Despite the many synonyms by which this ligament is recognized, and although there has been much effort directed toward adopting a universally acceptable or standardized name, the ligament is known best as Cooper's, after the anatomist surgeon who first described it. Cooper was the first to propose using this ligament in femoral herniotomy but actually Ruggi[16] (1893) was the first to suture the posterior edge of the anterior iliopubic ligament to the posterior iliopubic ligament. However, Annandale[2] (1876) had previously closed the femoral ring by obturation.

The ligament is deeply placed and extends from the iliopectineal eminence to the pubic spine. It is superimposed on the iliopectineal line or pecten of the pubes. It has a component which is adherent to the internal vertical surface of the superior pubic ramus. By using this portion of the ligament for attachment of the parietal wall, a wider approximation of the adjacent surfaces is obtained.

The ligament becomes thinner as it approaches the iliopectineal eminence. In rare instances, it becomes so attenuated laterally that insufficient fibers are available to hold securely the sutures used in attaching the fasciomuscular wall. Because of the strategic importance of the most lateral suture in preventing recurrence through the transitional space, Nicoll[14] drilled a hole through the pubic ramus for the passage of the suture; another ingenious method is to run the

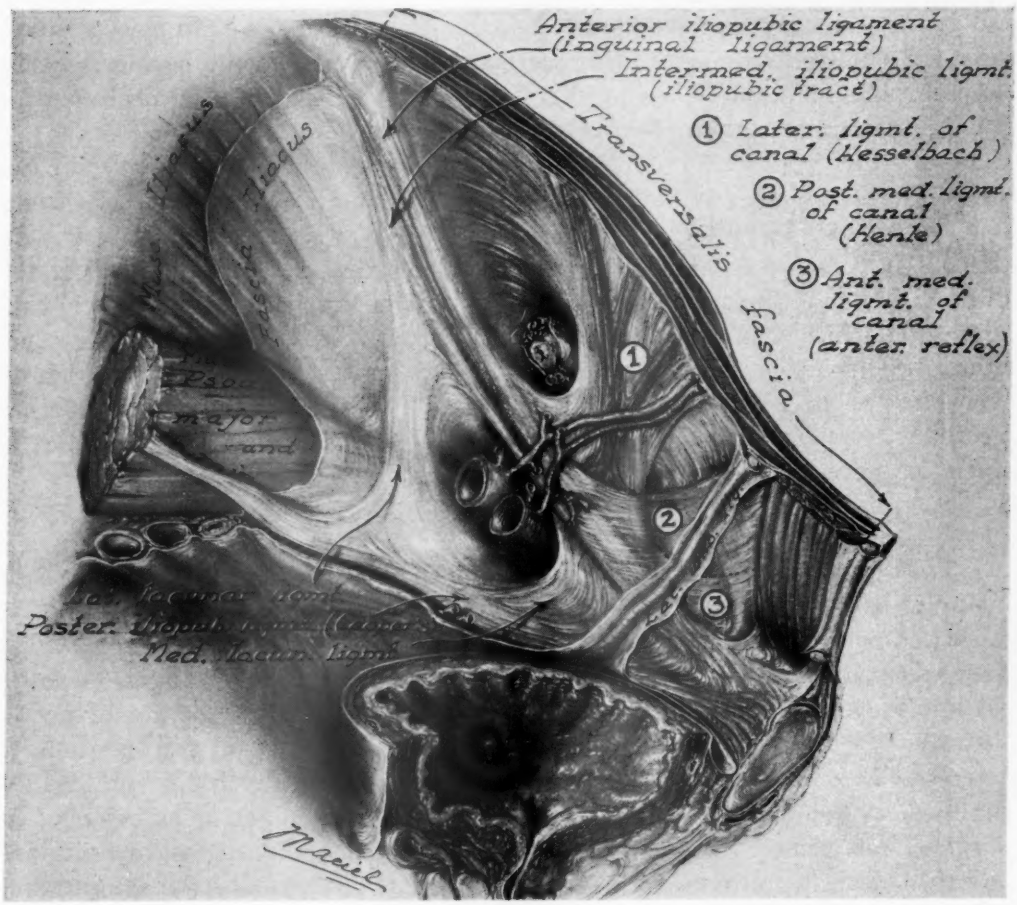


Fig. 2.—Sagittal section of the lower quadrant of the abdomen viewed from within outward. All nine ligaments of the inguinal region are shown in this composite drawing. The encircled numbers locate: (1) the lateral ligament of the floor of the canal (interfoveolar or Hesselbach's ligament), (2) posterior medial ligament of the floor of the canal (Henle's ligament), and (3) the anterior medial ligament of the floor (ligamentum inguinale reflexum). The lateral umbilical ligament, which actually is not intrinsic, pursues an oblique course and has been included in this category. The longitudinal ligaments of the inguinale region, anterior, intermediate and posterior iliopubic, and the auxiliary ligaments, the medial and lateral lacunar are labeled and easily recognized. The relationship of the spermatic cord, psoas fascia and muscles, and the external iliac vessels are illustrated.

suture around the ramus. Perhaps the simplest maneuver is to utilize either the expanded aponeurotic insertion of the psoas minor, if present, or the psoas fascia covering the major muscle directly beneath the external iliac vein. Should the lymph gland medially adjacent to the vein be enlarged, its removal will give increased accessibility of this region and better fascia-to-fascia contact.

The anterior surface of the ligament, in contrast to its vertical surface, is more constant, but a narrower contacting plane of the sutured structures ob-

tains and potentially a less strong union occurs than when the latter is used. Attempts to augment this area by reflecting the subjacent pectineal fascia and fibers have been disappointing.[3]

Since the most vulnerable part of a posterior iliopubic ligament repair is the transitional space where the repair changes from posterior iliopubic ligament to the anterior iliopubic ligament, it is essential that the surgeon be thoroughly familiar with the anatomic characteristics of the posterior iliopubic ligament and its relationship to the anterior iliopubic ligament if he is to meet successfully the challenge of obtaining a permanent cure of difficult hernias. Similarly, an anatomic knowledge of this ligament is indispensable in dealing with interligamentous or inguinofemoral hernias.

Since the criteria for the composite posterior iliopubic ligament repair are being interpreted more liberally, one is reasonably certain in predicting a wider adoption of this technique. The posterior iliopubic ligament ranks second in surgical importance among the ligaments of the inguina. It differs from the anterior iliopubic ligament in that its anatomic derivation is not intimately related to any mural stratum and, consequently, by reason of its independent position, it does not participate in the genesis of the weakness of the wall. Moreover, because of its increased and usually unyielding density and its deeper medial anatomic position, it affords a better diversional shunting of the intra-abdominal force, as has been pointed out by Lich and Samson.[11]

AUXILIARY ILIOPUBIC LIGAMENTS

Too often we are prone to learn the names of certain muscles and ligaments including their origin and insertion, but err by thinking of them unrelated to other anatomic structures. As a result, unless one possesses a retentive memory, they are soon forgotten. However, associating them with their clinical or surgical application imposes quite a different perspective. With the acceptance of the more objective concept there will be generated a purposeful and spontaneous interest. It is with this idea in mind that we have endeavored to present the practical aspect of these ligaments which are often thought of as being of no surgical importance. In our opinion they should be assigned to a definite and rightful clinical category second in strategic importance to the longitudinal ligaments of the inguinal region.

These vertically connecting and reinforcing bands bridging the interligamentous space are generally known as the medial and lateral lacunar ligaments. They augment the stability of the longitudinal iliopubic ligaments and, therefore, may in reality be considered auxiliary iliopubic ligaments.

Medial Lacunar Ligament (Gimbernat's or Inguinopectineal Medialis).—This ligament, which is triangular in shape, is interposed between the two major longitudinal ligaments of the groin, anterior iliopubic and posterior iliopubic ligaments. It is, in reality, a posterior reflection of the anterior iliopubic ligament, the continuity of which is easily recognized. It is constant and generally of uniform density. Its apex is beneath the pubic spine in conjunction with the anterior iliopubic, intermediate iliopubic, posterior iliopubic, posterior medial ligament and the anterior medial ligament of the canal. The ligament extends

laterally in an almost horizontal plane with its base forming the medial boundary of the femoral ring. The lateral extent of the ligament has been currently disputed by McVay and Anson[12] who contend that the fascia transversalis forms the medial boundary of the femoral ring except when the latter is dilated.

The functions of this ligament are the stabilization of the inferior margin of the anterior iliopubic ligament and the closure of the medial interligamentous space. It is conceivable that in those cases of hernia repair in which the anterior iliopubic ligament has been used exclusively for anchorage of the fasciomuscular wall, increased intra-abdominal pressure might cause cephalad pull

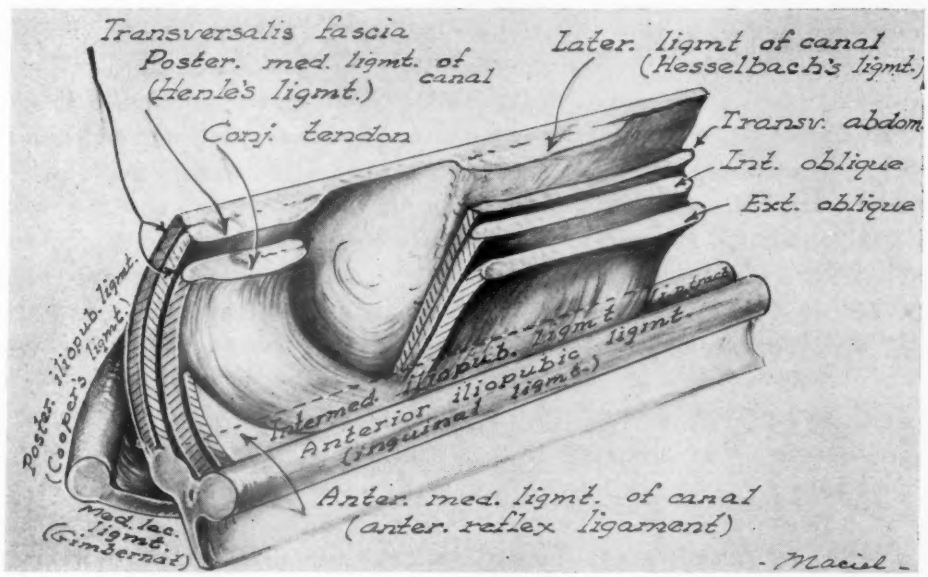


Fig. 3.—Cross section of the inguinal region suprajacent to the pubic tubercle. The relationship of the anterior iliopubic, intermediate iliopubic, and posterior iliopubic ligaments are shown as well as the medial lacunar, anterior medial and posterior medial ligaments of the inguinal canal. Attention is directed toward the posterior medial ligament of the floor of the canal (Henle's ligament) which is simply a thickening of the fascia transversalis. The transverse section supplements the anterior and sagittal views to further clarify the relationship of these ligamentous structures.

on the latter with possible widening of the interligamentous space. The medial lacunar ligament, therefore, would act as a check by exerting counter pressure and prevent widening of this space. Were it not for such a strong fascial membrane spanning the space between the pivotal ligaments, one could anticipate a higher incidence of interligamentous herniations than is presently reported. In those rare instances in which there is attenuation of the medial lacunar ligament, particularly if there is a concomitantly weak floor of the canal, there may occur a diffuse or elliptical oval bulging of the ligament, not unlike in many respects a direct dome-shaped hernia through the floor of the canal. In fact, these two types of hernias may coexist. A still rarer form of hernia is one making its exit through a small rent in the medial lacunar ligament. This diminutive cylindrical, usually fatty protrusion may not transmit an impulse and not infrequently is discovered coincidentally at operation. In this respect it is similar to a diverticular hernia through the cranial portion of the canal.

Important anatomically as is the medial lacunaar ligament in maintaining the integrity of the interligamentous space, it has never been employed in a reparative role. If the ligament is inadequate it may be excluded by attaching the musculofascial wall to the posterior iliopubic ligament; it can be reinforced with autogenous fascial sutures running between the inferior edge of the anterior iliopubic ligament and posterior iliopubic ligament, or as a third alternative, the cut edge of the anterior iliopubic ligament may be turned down and sutured to the posterior iliopubic ligament,[5] which in effect superimposes and replaces the medial lacunar ligament.

Lateral Lacunar Ligament (Inguinopectineal Lateralis).—There is paucity of knowledge as well as lack of complete agreement on the anatomic relationship of this ligament. Similarly, its surgical role is equivocal and its nomenclature is disputed. In some anatomy texts the ligament cannot be found; in others, it is illustrated but without an accompanying descriptive legend (Callander).[7] In Morris'[13] anatomy the ligament is depicted and its origin and relationship discussed very briefly. Although difficult to visualize at the operating table, it is easily palpated as an arcuate band of connective tissue of varying width extending from the inferior margin of the anterior iliopubic ligament obliquely downward to the posterior iliopubic ligament juxtalaterad the external iliac vessels and fanning out toward the iliopectineal eminence. It is intimately related to the psoas fascia and is probably augmented by some fibers of this fascia. Callander and Morris have referred to this ligament as the iliopectineal.

In the dissection preparatory to the usual or standard anterior iliopubic ligament hernia repair, the lateral lacunar ligament is not exposed or identified. Only in a posterior iliopubic ligament repair or in those cases in which the iliopsoas fossa is reinforced does the surgeon have the opportunity to observe this ligament. Its function, as one would expect, is to steady the anterior iliopubic ligament laterally by preventing it from spreading when subjected to increased pressure from within the abdomen or from inordinate parietal muscle contraction. Another equally important function is the division of the interligamentous space into a lateral lacunar musculorum and a medial lacunar vasorum, or medial and lateral inferior inguinal triangles.

It is reasonable to assume that if there were agenesis or attenuation of the lateral lacunar ligament, it would predispose to herniation through the lateral interligamentous space. Should there be concomitant weakness of the anterior iliopubic ligament, there is greater likelihood of bulging of the anterior wall of the lateral inguinal space.

Due to its inaccessibility and anatomic relationship, the lateral lacunar ligament does not lend itself to repair. However, where there is demonstrable bulging or weakness of the wall lateral to the external iliac vessels, I have described and illustrated a method of strengthening this occasionally vulnerable area by suturing jointly the anterior parietal wall strata to the medial edge of the psoas muscle beginning suprajacent to the abdominal ring and continuing downward along the edge of the recurved portion of the anterior iliopubic ligament.[6] This suture of autogenous fascia not only reduces the space but simul-

taneously creates a protective barricade lateral to the inguinal canal which diverts the intra-abdominal force away from the most vulnerable and likely site of recurrence of posterior iliopubic ligament repair.

LIGAMENTS OF POSTERIOR WALL OF INGUINAL CANAL

Those ligaments which augment the posterior wall of the canal fall in the third category. They are for the most part variations in the density of the fascia transversalis but may be comprised of other closely related mesenchymal, fascicular, or vascular elements. It is the latter contributing or adjunctive structures that give rise to much of the existing controversy and are chiefly responsible for the confusion and misunderstanding that persist among anatomists and surgeons. The lateral umbilical ligament is an exception in that it is not integrally related to the fascia transversalis and is of little strategic value.

The general direction of these ligaments is transverse to the longitudinal axis of the inguinal canal but they are variable and it does not necessarily follow that they are transverse to the long axis of the body; in fact, they are more commonly oblique in the latter relationship. Ordinarily, the lateral umbilical ligament when considered as a whole is vertical or oblique, but it deviates laterad inferiorly as it approaches the inguinal canal and may assume a transverse or oblique relationship to the canal. This observation can be verified at almost any hernia operation.

There are four ligaments of the posterior wall of the canal: ligamentum inguinale reflexum or anterior medial ligament of the canal, Henle's or posterior medial ligament of the canal, interfoveolar or lateral ligament of the canal, and the lateral umbilical ligament.

Anterior Medial Ligament of Inguinal Canal (Ligamentum Inguinale Reflexum, Triangular Fascia, or Colles' Ligament).—The anterior medial ligament of the canal bridges the small medial triangular space of the floor of the transparietal portion of the canal. Generally, it is easily recognized, when present, as a thin stratum of fascia superficial to the fascia transversalis, 1.5 to 2 cm. lateral to the pubic spine. Its derivation is from the medial reflection anteriorly of the recurved portion of the anterior iliopubic ligament which may blend with decussating fibers of the rectus sheath. Occasionally, it is separable from the underlying fascia transversalis. From my clinical and surgical experience, I am inclined to agree with Clark and Hashimoto who, in their anatomic dissections, have found this ligament so intimately related to the fascia transversalis that they consider it a variant of the latter. Perhaps one's point of view in regard to the origin of this ligament depends upon the acceptability of certain of the various controversial descriptions of the fascia transversalis.[18]

Perhaps because of its inconstancy, the anterior medial ligament has seldom been mentioned in operative procedures for hernias. An exception is Bisgard's[3] pedicled suture technique. He uses this ligament for transfixing the medial suture and has emphasized the necessity of its preservation in maintaining the integrity of the medial angle of the canal. In those cases requiring a more

formidable reparative procedure, such as the posterior iliopubic ligament repair, it may be advisable to divide the anterior medial ligament to gain adequate exposure of the medial third of the posterior iliopubic ligament.

Posterior Medial Ligament of Inguinal Canal (Henle's Ligament).—Because the posterior medial ligament is so variable in consistency, constancy, and size, most surgeons have long regarded it as of little practical importance; often it cannot be differentiated from the composite posterior fascial floor of the inguinal canal. Like other ligaments of this region, its derivation is not unitary. However, its origin is almost wholly from the fascia transversalis as a condensation of its fibers but it may also receive contributing bands from the contiguous rectus sheath and the overlying transversus aponeurosis. Despite its variability, the ligament characteristically is triangular in shape and occupies the medial third of the floor of the canal. If the anterior medial ligament is present, the posterior medial ligament is in a plane slightly beneath it and may extend 1 to 2 cm. lateral to its border but never as far as the medial boundary of the lateral ligament of the canal. Normally, the boundaries of these ligaments are almost imperceptible. Laterally, the posterior medial ligament often has no clearly definable anatomic marking. Consequently, there may be a variable gap of potential fascial weakness between it and the lateral ligament. The fascia transversalis is thinnest juxtacaudad the epigastric vessels. Accordingly, by the application of the principles of the dynamics of intraperitoneal pressure, Lich and Samson[11] found that the point where maximal force is exerted corresponds to the most vulnerable area of the floor. These coexisting factors of fascial attenuation and increased focal pressure continue to make this portion of the floor the most susceptible to herniation. Incidentally, this has been a long-recognized clinical observation.

Lateral Ligament of Inguinal Canal (Interfoveolar Ligament or Hesselbach's Ligament).—This ligament is the third and most lateral of the ligaments of the posterior wall of the inguinal canal, and is the most controversial of the three. It is situated near the superolateral extremity of the funicular canal and medially adjacent to the abdominal inguinal ring. It is longer obliquely, but narrower than, its two medial companion ligaments and spans and guards the base of the transitional space or trihedron. In the event the ligament becomes displaced, as frequently happens due to the hernial mass, it may present a concavity inferiorly or superiorly, depending on whether the hernia is indirect or direct. The ligament is composed chiefly of dense strands of fascia transversalis but some authorities have found, in addition, aberrant fascicular fibers of the transversus abdominis, which may add to its strength appreciably.

The inferior epigastric vessels lie subjacent and almost parallel to the lateral ligament. In addition to their vascular function they form the boundary between indirect and direct hernia. It is, therefore, imperative to identify the vessels in order to establish unequivocally which type of hernia is present. However, Browne[4] is opposed to the recognition of this age-old boundary concept of the epigastric vessels on the ground that they do not possess the tenseness and rigidity which would enable them to act as a dividing barrier. He contends

the ligamentous band which he has designated the internal crus of the abdominal ring is the stronger and the more logical anatomic structure to assume the role generally attributed to the inferior epigastric vessels. Accepting the concept of the most lateral ligament of the canal (interfoveolar) as having vascular, fascial, and fascicular components, would provide a logical means by which long-existing differences of opinion could be resolved, and would lead to a clearer understanding of this important composite structure.

Lateral Umbilical Ligament of Inguinal Canal (Hypogastric Remnant).— In the process of embryological evolution of the structures of this region, the distal portions of the hypogastric arteries, from the bladder to the umbilicus, collapse after cessation of the placental circulation at birth and revert to easily identifiable subperitoneal cords. Anson and co-workers have found that these remnants are from 0.5 to 1 cm. medial to the femoral ring. They almost invariably require dissection from the inferior convex surface of the direct hernial sac suprajacent to the bladder during the saccular mobilization. With the surgeon's finger in the opened sac, a cordlike band can be felt running obliquely or transversely across the floor of the canal medial to the inferior epigastric vessels. It is relatively mobile and may be displaced by the hernial mass.

The principal significance of the hypogastric fibrous cords is that of an anatomic marker between the supravesical and middle inguinal fossae. They differ from the other ligaments of the canal in that they do not arise from expansion or condensation of fascia, as is usually implied by the term ligament. Whether their support of the posterior wall of the inguinal canal justifies their inclusion in the category of intrinsic ligaments of the inguina may be open to legitimate differences of opinion.

SUMMARY

1. The anatomic, clinical, and surgical aspects of the intrinsic ligaments of the inguinal region have been discussed in the light of our present knowledge. The objective has been to gain a better practical understanding of them when applied in the surgical management of that common, and too often disabling, malady, inguinal hernia.

2. The preferable anatomic nomenclature has been given first, followed by its synonyms. Special effort has been made toward the abandonment of the use of proper names. How successful this well-intentioned effort is destined to be depends upon the continued emphasis on the correct anatomic name by anatomists and surgeons alike in their teaching and their publications.

3. In the evaluation of the ligaments of the groin, nine have been described, five of which are inferior to the inguinal canal and four reinforcing the posterior wall of the canal. It should be noted that the three longitudinal ligaments, the medial lacunar, anterior medial, and posterior medial ligament all have a common insertion into the pubic spine.

4. The ligaments of the inguina have been classified in three distinct categories: longitudinal iliopubic, auxiliary iliopubic, and ligaments of the posterior wall of the inguinal canal.

5. Perhaps other explanations, aside from the complicated nomenclature, as to why the surgeon is unable to retain certain ligaments of the inguinal region in mind are the inconstancy of the anterior medial ligament and posterior medial ligament, and the inability of the surgeon to visualize at operation the intermediate iliopubic and lateral lacunar ligaments.

REFERENCES

1. Anson, Barry J., Reimann, Arthur F., and Swigart, LaVerne L.: The Anatomy of Hernial Regions, II. Femoral Hernia, Surg., Gynec. & Obst. **89**: 753-763, 1949.
2. Annandale, T.: Direct Inguinal and Femoral Hernia, Edinb. M. J. **21**: 1087-1091, 1875-1876.
3. Bisgard, Dewey J.: The Use of Giving Sutures of the External Oblique Aponeurosis in the Repair of Inguinal Hernias in Adults, Surg., Gynec. & Obst. **68**: 113, 1939.
4. Browne, Dennis: Some Anatomical Points in the Operation for Undescended Testicle, Lancet **1**: 460, 1933.
5. Burton, Claud C.: The Criteria, Classification and Technique of Iliopectineal (Cooper's) Ligament Hernioplasty, Surg., Gynec. & Obst. **89**: 227-236, 1949.
6. Burton, Claud C.: Use of the Iliopsoas and Autogenous Fascias in the Repair of Certain Inguinal and Femoral Hernias, SURGERY. In press.
7. Callander, Latimer: Surgical Anatomy, Ed. 2, Philadelphia, 1940, W. B. Saunders Company, p. 703.
8. Clark, John H., and Hashimoto, Edward I.: Utilization of Henle's Ligament, Iliopubic Tract, Aponeurosis Transversus Abdominis and Cooper's Ligament in Inguinal Herniorrhaphy, Surg., Gynec. & Obst. **82**: 480-484, 1946.
9. Cooper, Astley: The Anatomy and Surgical Treatment of Inguinal and Congenital Hernia. London, 1804.
10. Dugdale, F. E., and Burton, Claud C.: The Surgical Triangles of the Inguinopectineal Region (Inguina): Their Classification, Parietal Relationship and Significance in Hernia Repair, Ann. Surg. **127**: 627-639, 1948.
11. Lich, Robert, Jr., and Samson, Ralph B.: A Method of Inguinal Herniorrhaphy, Internat. Coll. Surgeons **8**: 454-458, 1945.
12. McVay, Chester B., and Anson, Barry J.: Inguinal and Femoral Hernioplasty, Surg., Gynec. & Obst. **88**: 473-485, 1949.
13. Morris, Henry: Morris' Human Anatomy, ed. by J. Parsons Schaeffer, Ed. 10, Philadelphia, 1942, The Blakiston Company, pp. 531, 1337.
14. Nicoll, James H.: The Radical Cure of Femoral Hernia. A Modification of the Author's Operation, Scot. M. & S. J. **13**: 511-522, 1903.
15. Quain's Anatomy: London, 1922, **4**: Part II, 204.
16. Ruggi, Giuseppe: Del Metodo Inguinale, Nella Cura Radicale, Dell'Ernia Crurale. Bologna, 1893, Ditta Nicola Zanichelli.
17. Sellig, M. D., and Tuholske, Lister: The Inguinal Route Operation for Femoral Hernia: With a Supplementary Note on Cooper's Ligament, Surg., Gynec. & Obst. **18**: 55-62, 1914.
18. Tobin, Charles E., Benjamin, John A., and Wells, John C.: Continuity of the Fascia Lining and Abdomen, Pelvis, and Spermatic Cord, Surg., Gynec. & Obst. **83**: 575-590, 1946.

SQUAMOUS-CELL CARCINOMA OF THE FLOOR OF THE MOUTH

WALTER L. MATTICK, M.D., DONALD J. MEEHAN, M.D., AND
JOHN P. HABERLIN, M.D., BUFFALO, N. Y.

(From the Roswell Park Memorial Institute)

SQUAMOUS-CELL carcinoma of the floor of the mouth is an infrequent form of cancer, yet poses many problems for the surgeon. Since radical surgery is being employed more frequently at the present time[1, 2] for intraoral cancer it is important to have comparative studies of radiation-treated series. It is our purpose to evaluate the results of treatment by radiation alone in 82 patients with proved squamous-cell carcinoma of the floor of the mouth. In this series there was no instance of definitive surgery performed for the purpose of completely excising the cancer. The primary lesion and neck node metastases were treated entirely with radiation in some form. The years 1937 to 1945, inclusive, were chosen for study because all the latest radiologic techniques were available during this period.

The importance of careful anatomic classification of intraoral cancer cannot be overemphasized. Carcinoma of the lip, floor of the mouth, gum, tongue, buccal mucosa, palate, tonsil, and tonsillar pillars all present different problems in treatment, management, and prognosis. The results, therefore, should be reported separately. Only when this policy is adhered to can accurate comparative studies be made.

In the years 1937 to 1945, inclusive, 98 patients with squamous-cell carcinoma of the floor of the mouth were examined at this Institute. Out of this group, 82 patients were suitable for statistical evaluation. The remaining 16 patients were clinic shoppers (seen but not treated), individuals who had treatment elsewhere and were seen only for further consultation, and those lost to follow-up under 5 years, but free of disease when last seen. All other cases, regardless of the extent of the disease, were treated and are included in the study. In order to insure standardization of statistics and allow comparison only squamous-cell carcinomas are reported. The clinical course of tumors other than squamous-cell carcinomas is so different that accurate comparison cannot be made.

Incidence.—During the years 1937 to 1945, inclusive, 16,704 patients with cancer were seen at the Roswell Park Memorial Institute. Carcinoma of the floor of the mouth represented 0.6 per cent of all cancer and 17 per cent of intraoral cancer seen in this Institute. Martin and Sugarbaker[3] reported that carcinoma of the floor of the mouth represented 1.43 per cent of all cancer.

Color.—All patients in this series were white; no Negro patients with this disease were seen. In a group of 418 carcinomas of the tongue, gum, and floor

Received for publication, Sept. 7, 1951.

of the mouth the incidence of Negro patients in this Institute was 0.5 per cent. This city is a northern city with a very small Negro population, about 5 per cent. Our Negro percentage, nevertheless, is much below the expected figure.

Age.—Intraoral cancer is definitely a disease of the older age groups. The majority of the patients in this series were well over 50 years of age. The decade with the greatest incidence (Table I), was 51 to 60 years. The youngest patient was 44 and the oldest 84 years old. The median age was 61 years.

TABLE I

	TOTAL CASES	FIVE-YEAR CURES	FIVE-YEAR CURE RATE (PER CENT)
Age			
41-50	14	1	7
51-60	27	7	26
61-70	19	4	21
70	22	3	14
Sex			
Men	79	15	19
Women	3	0	0
Color			
White	82	15	18
Other	0	0	0
Position		7	18
Anterior	38		
Left	25	4	16
Right	19	4	21
Pathology		6	16
Grade I	37		
Grade II	38	8	21
Grade III	7	1	14
Metastases			
No nodes on admission	31	11	35
Nodes on admission	45	1	2
Developed nodes	18	3	17
No nodes at anytime	19	11	58

Sex.—Men were in the overwhelming majority in this series, comprising 97 per cent of the total cases. Other reports[3] also place the incidence among men of carcinoma of the floor of the mouth higher than that of any other intraoral cancer. In comparison, our figures[4] for the incidence among men of carcinoma of the gum is 76 per cent, and for carcinoma of the tongue 80 per cent.

Serology.—Fifty-five of the patients in this series had a positive serology on admission. The average incidence of positive serology in routine admissions to a general hospital in this city is about 5 per cent. From these figures it would not seem that syphilis had any role as precursor in carcinoma of the floor of the mouth. In contrast to this there was an 18 per cent incidence of positive serology in 235 cases of tongue cancer at this Institute.

Oral Hygiene.—The majority of our patients used tobacco and displayed some form of poor oral hygiene, often in the form of pyorrhea and caries or loose and ill-fitting dentures. Many patients consulted their dentist because they thought their trouble was dental in origin. Leukoplakia of the floor of the mouth was seen frequently. Several patients described their lesions as arising from a previously existing "white patch." On examination, the leuko-

plakia could at times be seen at the border of the carcinoma. We feel that leukoplakia is a precursor of cancer in a small percentage of cases and when this condition is diagnosed, the patient should be followed and biopsies taken from any suspicious area. The treatment of leukoplakia is a difficult subject and not within the scope of this paper.

Lymphatics.—According to Rouviere,[5] the lymphatic network of the floor of the mouth is continuous with that of the tongue and the gum. The floor of the mouth, therefore, shares the same nodal connections as the lingual lymphatics. The lymphatics of the anterior floor of the mouth covering the sublingual gland are drained by the nodes which drain this gland. The sublingual gland itself is drained by the submaxillary nodes and superior jugular nodes. From the foregoing, it can be seen that the jugular nodes and submaxillary nodes are the main routes of lymphatic spread. Clinically, the submental nodes are seldom involved.

Position.—The floor of the mouth is U-shaped and covered by stratified squamous epithelium. On each side posteriorly, the floor begins approximately at the junction of the tongue and anterior tonsillar pillar. It is bounded laterally and anteriorly by the lower gum and medially by the undersurface of the tongue. In this study the lesions have been classified as right, left, and anterior floor of the mouth. Thus, the lesions which remained entirely unilateral were classified as right or left, depending on their site. Lesions crossing the midline were designated as anterior. Figs. 1 and 2 illustrate anterior and side floor of the mouth lesions. Forty-six per cent of the 82 cases were considered as anterior lesions. Of the remainder, 30 per cent occurred on the left side and 24 per cent on the right. The cure rate varied only slightly (Table I), and it is therefore apparent that factors other than position play a more important part in prognosis. The anterior cancers have the advantage of being more accessible to diagnosis, biopsy, and treatment so that one might expect the best results with this group. On the other hand, they are more likely to have bilateral neck node metastases, which would counteract the former advantage. In the following discussion, it will be seen that the extent of the disease has the greatest influence on the ultimate prognosis.

Pathology.—This group is composed entirely of squamous-cell carcinomas. All cases were reviewed and the original diagnosis confirmed. The slides were graded, using a modified Broders' Classification. Grade I consists of the usual Broders' I and our Grade II comprises Graded II and III of Broders' classification. Grade III corresponds to Broders' Grade IV. Approximately 90 per cent of the cases fell into Grades I and II, with an equal percentage in each grade.

Table I shows the five-year cure rate according to grade. The low 14 per cent five-year cure rate for Grade III is insignificant, considering the small group in this grade. There is an even wider range in the cure rates between Grades I and II than between Grades I and III, the so-called differentiated and undifferentiated squamous-cell carcinomas. Therefore, no conclusion can be drawn from this series in regard to grade and prognosis.

Metastases.—It has been our experience that metastatic neck nodes constitute one of the most important prognostic features in intraoral cancer.[4] Table I shows that only 2 per cent (1 out of 45 cases) of the patients who had metastatic neck nodes on admission survived five years. Seventeen per cent (3 out of 18) of the patients who developed metastatic neck nodes later in the course of follow-up survived five years or over. These cases were all treated with some form of radiation. The five-year cure rate for those patients who never developed neck nodes was 58 per cent. This figure represents all cases without nodes regardless of the size of the primary lesion. The cure rate of 35 per cent in Table II represents the five-year cure rate in those patients with carcinoma of the floor of the mouth but no metastatic neck nodes on admission. Averaging all patients with neck nodes, i.e., 63 patients, the five-year cure rate is

Fig. 1. Fig. 2.

Fig. 1.—Photograph showing a lesion of the right floor of the mouth. Biopsy revealed a squamous-cell carcinoma.

Fig. 2.—Typical cauliflower carcinoma of the anterior floor of the mouth.

6 per cent. Incidentally, there were no patients in this series that had distant metastases without evidence of metastatic neck nodes. We have no figures for the percentage of people dying with distant metastases. Most of our cases came from quite a distance, so that we did not see them in the terminal phase of their disease.

Treatment.—All cases treated in this series received radiation in some form. Several techniques were used. Interstitial radiation in the form of radon seeds or radium needles was combined with external x-radiation, using the 200 kv. x-ray, half-value layer 0.9 mm. Cu. Another technique consisted of a mouth mold loaded with radium calculated to deliver a surface dose of 6000 gamma

roentgens (500r × 12). This was followed with a course of external radiation as stated previously. Another technique used in the later years was the intraoral method, often combining this with an external port. No conclusion can be drawn from these techniques since the breakdown of cases would necessarily make the groups too small to be of statistical value. We do believe, however, that all methods and techniques have their own advantages and limitations. The intraoral method probably was used mostly in the more recent years. Metastatic neck nodes were treated entirely with radiation. The usual method was using the 200 kv. machine, half-value layer 0.9 mm. Cu., using multiple ports over the affected node-bearing area. At times it was possible to treat the primary lesion and nodes through a single port. Radon seeds, inserted in the nodes as supplemental radiation, were used in many cases.

TABLE II. FIVE-YEAR END RESULTS 1937 TO 1945, INCLUSIVE

Total Number of Cases		98
Indeterminate Group		
Dead of other causes without recurrence	8	
Seen but not treated, or treated elsewhere	8	
		16
Determinate Group		82
Failures		
Dead as a result of cancer		67
Successful Results		
Free of disease 5 years or more		15
Net Five-Year Cure Rate		
Successful results divided by determinate group (15/82)		18%
Early cases, i.e., no node involvement on admission		35%

Complications.—The usual radiation reactions were experienced at this Institute. When administering large cancericidal doses of radiation this often cannot be avoided. Careful attention to oral hygiene, condition of the teeth, and radiation technique can minimize these difficulties. We made no attempt to determine the radiation complications in the patients who died of the disease. In the 15 cured patients there were 6 complications severe enough to be recorded on the hospital charts. There was one patient with severe pain over the treated floor of the mouth. The mucosa was scarred, telangiectatic, and very tender. Five patients had radio-osteomyelitis of the mandible. This is a complication very difficult to prevent in many cases. Where large lesions abut against the alveolar ridge, treatment of necessity opens pathways of infection down to the bone which, combined with the radiation effect, produces the entity of radio-osteomyelitis. In four of these patients, eventually the sequestrum extruded and the exposed mandible became covered with mucosa. One patient in this series had a severe radio-osteomyelitis that fractured the mandible and produced an oral fistula. He had a very large lesion with metastatic neck nodes and received heavy doses of radiation. He is still alive today and only slightly inconvenienced by the oral fistula. At this point we should like to stress the importance of good general medical care during radiation therapy. These patients are somewhat malnourished and anemic. Their mouths are tender and painful from the cancer and radiation reaction. Careful check of their general condition with supplementary feedings, iron, liver extract, or even transfusions is essential to a successful outcome.

Results.—Again we wish to emphasize that all the cases in this series were treated with radiation alone. The cure rate for the 82 cases in the determinate group was 18 per cent. This group includes all cases treated at this Institute. The five-year cure rate for those patients who had no neck nodes on first examination was 35 per cent. Martin and Sugarbaker, in 1940,[3] reported a 25 per cent cure rate for 103 patients with carcinoma of the floor of the mouth. Melville,[6] reporting on 69 patients, combined lower gum and floor of the mouth lesions and obtained a 45 per cent three-year cure rate. Our results for all cases with metastatic neck nodes show a 6 per cent five-year cure rate. Martin and Sugarbaker[3] reported a 22 per cent five-year cure rate in patients with neck node metastases. This figure, however, is the result of both radiation and radical neck dissection.

Surgery.—In recent years, following the experience of the Memorial Hospital and Johns Hopkins group, and papers by Ward,[7] Slaughter,[1] Watson,[8] and Sugarbaker[2] interest has been aroused in the treatment of intraoral cancer by radical surgery. The results of radiation appear to justify a renewed surgical attack on intraoral cancer. From the results of our study we have realized that certain cases have a poor prognosis when treated with radiation. Our work over the past few years has centered mainly on this type of patient. In a recent study[4] we found no five-year cures in gingival cancer when the underlying bone was involved. Slaughter[1] had no cases of intraoral cancer with bone involvement surviving more than 18 months. Therefore, it has been our feeling that invasion of the mandible by cancer of the floor of the mouth is a definite indication for a radical resection of the floor of the mouth, mandible, and neck nodes. Since the results of radiation are so poor when the neck nodes are involved by metastatic squamous-cell carcinoma (Table I), we also feel that this same radical jaw and neck dissection offers the most efficient means of excising the lesion and its regional nodes. Another problem that may become a surgical one is the radiation failure. The patient who despite an adequate course of radiation has persistent disease is almost always doomed. We have had the experience, however, on several occasions, of irradiating an inoperable intraoral cancer and find that the radiation, though it has not sterilized the lesion, has shrunken it to a resectable stage. It is also important to note the relief of pain afforded by the radical jaw and neck dissection. The patient suffering from uncontrollable intraoral cancer is a pitiful sight. We have resected many massive cases of this type following an unsuccessful attempt at cure with radiation. The pain relief has been most satisfying. Several patients have been returned to a useful occupation following surgery. True, we have had recurrences and death, but here again, pain has been negligible even in the terminal stage. We do not mean to imply the indiscriminate use of surgery, cutting through cancer tissue, or complete disregard of tried and true cancer principles. A surgical and medical judgment must be combined with a knowledge of the process of intraoral cancer.

Our technique differs only slightly from that described by Slaughter and associates. The operation begins with a radical neck dissection. As the dissection reaches the beginning of the external carotid artery this vessel is tied in

continuity just above the superior thyroid artery. The lip is then split in the midline and the lower jaw transected at the desired point. After the mandible is sectioned the submaxillary dissection is then very quickly performed along with the removal of involved intraoral tissue. The entire specimen is removed in one piece. The repair of the mouth and closure of the neck follows the technique of Slaughter. This method has its greatest usefulness for lesions of the gum and side floor of the mouth. Fig. 3 shows the patient postoperatively. There is a relatively minor facial deformity. However, since floor of the mouth cancer involves the anterior floor in 50 per cent of the cases, the anterior jaw must frequently be resected. This results in the Andy Gump deformity depicted in Fig. 4. We feel that in the selection of these cases the chances for cure or palliation must be carefully weighed against the surgical deformity.

Fig. 3. Fig. 4.

Fig. 3.—Postoperative photograph, 2 months after a left combined jaw and neck dissection. Note the minimal cosmetic deformity.

Fig. 4.—This patient had a squamous-cell carcinoma of the floor of the mouth recurrent after radiation therapy. A bilateral submaxillary dissection plus resection of the anterior jaw and floor of the mouth was done. There is no evidence of recurrence at present.

A major postoperative problem that fortunately occurs rarely is that of oral fistula. In our cases the only oral fistulas were in those cases with extensive lesions in which we have had to sacrifice large amounts of skin or in those which were postradiation failures. Without adequate skin coverage of the oral suture line, or where irradiated scarred mucosa and skin are closed, fistulas are bound to occur occasionally. Small fistulas are not too troublesome and are fairly well controlled with a small gauze patch. If the patient does well for six months or so, the fistula may be repaired in many ways, such as with sliding flaps or pedicled tubed transplants.

SUMMARY

Eighty-two cases of squamous-cell carcinoma of the floor of the mouth are reported. All cases were treated with radiation, in some form, to both primary and metastatic neck nodes. The five-year cure rate for the entire group was 18 per cent. The five-year cure rate for those cases without neck node involvement on admission was 35 per cent. Approximately 45 per cent of the cases in this series had no nodes on admission but half of these cases eventually

developed them. Those patients with neck node metastasis on admission and patients with extension of their cancer into the lower jaw appear to warrant an attempt at surgical extirpation of their cancer.

We have made no attempt to delve into the problems of prophylactic neck dissection or the surgical treatment of metastatic neck nodes when there is a healed primary lesion.

REFERENCES

1. Slaughter, D. P., Roeser, E. H., and Smejkal, W. F.: Excision of the Mandible for Neoplastic Disease, SURGERY **26**: 507, 1949.
2. Sugarbaker, E. D., and Gilford, J.: Combined Jaw Resection-Neck Dissection for Metastatic Carcinoma of the Cervical Lymph Nodes, Secondarily Involving the Mandible, Surg., Gynec. & Obst. **83**: 767, 1946.
3. Martin, H. E., and Sugarbaker, E. D.: Cancer of the Floor of the Mouth, Surg., Gynec. & Obst. **71**: 347, 1940.
4. Mattick, W. L., and Meehan, D. J.: Carcinoma of the Gum, SURGERY **29**: 249, 1951.
5. Rouviere, H.: Anatomy of the Human Lympathic System, Ann Arbor, Mich., 1938, Edwards Brothers, Inc.
6. Melville, A. G. G.: Double Radium Mould Treatment of Carcinoma of the Floor of the Mouth and Lower Alveolus, Brit. J. Radiol. **13**: 337, 1940.
7. Ward, Grant E., and Hendrick, James W.: Diagnosis and Treatment of Tumors of the Head and Neck, Baltimore, Md., 1950, Williams & Wilkins Company.
8. Watson, Wm. L.: Radical Surgery for Head and Neck Cancer, New York State J. Med. **51**: 2631-2636, 1951.

Case Reports

HEPATIC PORTAL ARTERIOVENOUS FISTULA

A Case Report

J. H. Strickler, M.D., Nathaniel Lufkin, M.D., and Carl O. Rice, M.D.,
Minneapolis, Minn.

IT WOULD seem a singular coincidence that at approximately the same time that Schilling, McKee, and Wilt[17] first reported their studies of the experimental production of hepatic portal arteriovenous fistulas, a clinical case was also encountered at the St. Barnabas Hospital. A survey of the literature indicates that the case reported here is unique.

The presence of normal arteriovenous connections or anastomoses within the liver has been demonstrated by several investigators. By a technique of transillumination of the liver in situ, Wakin and Mann[23] found anastomoses between the interlobular branches of the hepatic artery and portal vein. Dumais[7] injected a plastic material into the vessels and then digested the parenchyma away from them. In this manner similar shunts were demonstrated. Seneviratne[19] confirmed the findings of Wakin and Mann by employing a similar technique in a study of frog, mouse, and rat livers. Prinzmetal and associates[15] injected glass spheres of much larger than capillary size (50 to 180 microns), however, since the injection was made into the portal vein and the spheres recovered from the hepatic vein they actually demonstrated a veno-venous shunt in the liver.

The problem of ascites as related to portal vein pressure has been studied from various approaches. In experimental studies, Volwiler, Bollman, and Grindlay[21, 22] concluded that venous congestion of the liver followed by constriction of the vena cava above the liver produces a rapid ascites. They compared this situation to that of hepatic vein thromboses or Chiari's syndrome and to constrictive pericarditis, and to congestive heart failure. Such an ascites had a high protein content. They also found that a complete ligation of the main portal vein in two stages in the dog did not result in chronic portal hypertension. Boyce,[6] previously had pointed out that a staged occlusion of the portal vein could be tolerated. Gerbode and associates[8] made azygous vein shunts and anastomoses of superior vena cava to right auricle in studying the problem of superior vena caval obstruction.

Schilling, McKee, and Wilt,[17, 18] by a very ingenious method, were able to anastomose the hepatic artery to the portal vein in dogs. They were able to find no elevation of venous pressure, no congestion of mesentery, or any cardiovascular embarrassment. They also concluded that the development of ascites required obstruction within the hepatic veins of the liver or of the vena cava above it. Kunkel and Eisenmenger,[10] on the other hand, found that some ascites

Received for publication, March 16, 1951.

could be produced in rats by partial obstruction of the portal vein below the liver. The amount of ascites did not seem to correlate well with the degree of portal hypertension.

Snell[20] has commented upon the multiple factors involved in the production of ascites. These factors include increased portal vein pressure, lowered osmotic pressure of serum incident to a reduction of the serum albumin, disturbances in lymphatic flow, such as are caused by constriction of the hepatic vein, excessive antidiuretic factor, vasodepressor mechanism, and electrolyte metabolism.

Rousselot[16] emphasized the anatomic variation of the coronary vein as a deciding factor in the choice of surgical treatment of congestive splenomegaly due to splenic vein thrombosis. When the coronary vein enters the portal vein, a splenectomy will suffice, but when the coronary inlet is blocked by entrance into a thrombosed splenic vein then a splenorenal shunt must also be done to relieve the tendency to esophageal varix formation.

As early as 1907 Herrick[9] found that hepatic arterial pressure had a profound influence on portal vein pressure in perfused cirrhotic livers. Berman and associates[1] have attacked the problem of ascites formation by ligation of the origin of the hepatic and splenic arteries in experimental animals and some patients.

In 1945, Whipple[25] reviewed completely the background work on the problem of portal hypertension prior to and including the initial development of shunt procedures. In 1951, Markowitz and Rappaport[13] reviewed current problems pertinent to hepatic arterial circulation.

The clinical and pathologic findings of a case observed at the St. Barnabas Hospital are reported in detail in order that these findings might be compared with others which might be observed in the future.

CASE REPORT

H. C., a 49-year-old white woman, was first examined on June 17, 1949, six weeks after she had first noted a protuberance of the abdomen. The distention had been slight and had disappeared and reappeared on several occasions during that time.

A gastrointestinal x-ray series on June 28, 1949, was negative. This included a search for esophageal varices.

The first paracentesis was done on Aug. 4, 1949. The sediment failed to reveal malignant cells. Then ten days later it was necessary to repeat the paracentesis in order to give the patient comfort. Twenty-five hundred ml. of fluid were withdrawn.

The fluid contained a considerable number of polymorphonuclear leukocytes. Specific gravity was 1008, protein 1.7 Gm. per cent. Serum proteins were 7; albumin 4.2; globulin 2.8; serum bilirubin 1 minute 0.04, total 0.12; bromsulfalein retention 30 minutes 8 per cent and 60 minutes 3 per cent; urine urobilinogen 0.2 Ehrlich unit.

The hemoglobin was brought from 54 per cent to 90 per cent by whole blood transfusions and then, since it was felt that the usual clinically encountered causes of ascites had been ruled out, with the exception of remaining doubt concerning a possible ovarian carcinoma, a laparotomy was performed on Aug. 18, 1949.

The peritoneal cavity contained approximately 2,000 c.c. of pale, straw-colored fluid. The liver appeared to be somewhat anomalous in its contour. The left lobe occupied almost all of the liver space. The gross appearance suggested normal liver parenchyma. The gall

bladder was found to be situated posteriorly and laterally. The foramen of Winslow could not be found. There were no outward evidences of portal hypertension. The root of the mesentery of the small intestine was edematous.

A liver biopsy revealed some increased fibrous tissue in the portal spaces, but there was no change characteristic of cirrhosis. The postoperative course was uneventful and the patient was discharged on Aug. 28, 1949.

On the following day four liters of fluid were removed from the peritoneal cavity by parancentesis possessing a specific gravity of 1008 and 1.7 Gm. per cent of protein.

The patient was readmitted on Sept. 2, 1949, having vomited bright red bright.

Paracentesis was again performed on Sept. 2, 1949, obtaining 5,300 c.c. of fluid containing 1 Gm. protein and specific gravity of 1008.

The intestinal bleeding ceased after 36 hours of transfusions during which time approximately 7.5 liters of blood were given. The total proteins taken on Sept. 6, 1949, were 5.7, albumin 3, globulin 2.7, cephalin cholesterol 24 hours negative, 48 hours plus one, blood urea nitrogen 9, chlorides 542 mg. per cent.

The patient was placed on a high protein, salt-free diet (350 mg. sodium) directed toward suppression of the ascites formation.

Bromsulfalein excretion showed 15 per cent retention in 45 minutes. It was thought that this might possibly represent some slight temporary liver damage following severe hemorrhage.

A medical consultant was of the opinion that the bleeding was due to esophageal varices.

On Sept. 14, 1949, it was necessary to repeat the paracentesis and 3,500 c.c. were obtained.

On Sept. 21, 1949, a urine urobilinogen determination revealed 1.4 mg. per day. Total proteins were 5.4, albumin 2.8, and globulin 2.6. Serum bilirubin was 0.12 in 1 minute with a total of 0.96.

On Sept. 22, 1949, bleeding recurred with a hemoglobin drop to 40 per cent.

This second occurrence of massive bleeding, approximately three weeks after the first one, was of similar severity, requiring 4.5 liters of blood, but the patient's general condition was not quite as satisfactory.

A splenorenal or portacaval shunt operation, as described by Blakemore,[2-4] Blalock,[5] Linton,[11, 12] and Whipple[25] was considered, but before further build-up and decision could be made the patient had had her third incident of spontaneous hematemesis and profound shock on Oct. 6, 1949.

She was again transfused and after four days of very severe bleeding, during which several drops of blood pressure to zero and an imperceptible pulse had occurred, it was decided that only an immediate radical procedure could save the patient. Eight liters of blood were used and as soon as a normal blood pressure had been obtained and maintained for approximately one hour under pressure transfusion, a laparotomy was performed on Oct. 9, 1949.

A subtotal gastrectomy, as suggested by Wangensteen[24] was considered since in addition to interrupting the coronary-esophageal anastomosis, the acid factor could also be eliminated. However, it was feared that the patient might not tolerate prolongation of the procedure, therefore, a devascularization procedure was employed as an alternative. Approximately 5 of each 6 vessels were ligated on the upper half of the stomach and lower 1 inch of esophagus. The stomach was opened and a large clot, a cast of the esophagus, was evacuated.

The patient appeared quite normal eighteen hours after surgery. The urine ouput was normal.

On the first postoperative day the patient developed mild pulmonary congestion. A moderate degree of heart failure was evident, probably caused by the tremendous exchange of fluids the patient had to undergo prior to and during surgery.

A moderate oliguria developed in postoperative days one through five. An isosthenuria of 1012 pertained. PSP excretion on Oct. 13, 1949, was 11 per cent in two hours. Bromsulfalein retention was 17½ per cent in forty-five minutes. The serum bilirubin had grad-

ually risen in the past three weeks to 1.04 in one minute with a total of 1.92. Cephalin cholesterol was two plus in 24 hours and a few days later was three plus. Alkaline phosphatase was 25.5 King Armstrong units. Prothrombin time was 13.5 against a control of 12.5.

There was rapid reaccumulation of fluid in the peritoneal cavity after operation which required repeated paracenteses.

The blood urea nitrogen after operation rose to 211 within a few days and the creatinine rose to 3.5.

Slight sacral edema became evident and in spite of the low chloride (434 to 458) salt was restricted to 4½ Gm. a day, but disappeared in 2 days. The total fluid intake then was restricted to 1,500 c.c. a day by intravenous injection on a working diagnosis of lower nephron nephrosis. Five hundred c.c. of plasma were given daily in addition to the 1,500 c.c. of 20 per cent glucose fluid. A diuresis (2,800 ml.) finally occurred on Oct. 17, 1949. The mental state remained more or less unchanged in moderate confusion. Pulse remained normal. There was no more evidence of additional bleeding after the operation.

The clinical picture, however, did not improve in spite of the electrolyte balance returning to normal. The patient became progressively more comatose, and died on Oct. 18, 1949.

Pathologic findings.—The findings at post-mortem examination were not significant, except as follows:

The liver was found to be enlarged (1,900 Gm.) and grossly abnormal in configuration. The falciform ligament was found to be at about the right midclavicular line. The foramen of Winslow was located only after deflecting the liver medially and anteriorly. It was found to be medial to the anterior axillary line.

Using the falciform ligament as the dividing line between right and left lobes of the liver it was found that the left, including the caudate and quadrate lobes, was larger than the right. The left lobe measured 24 cm. at the point of greatest height and 14 cm. in width. The right lobe was 21 cm. in height and 12.5 in width. The quadrate lobe was also enlarged, measuring 8.5 cm. from the falciform ligament to the gall bladder fossa.

Further dissection of the liver to demonstrate the main branches of the portal veins and to determine to course of the large and tortuous hepatic artery showed a startling picture (see Fig. 1).

Both the right and the left main branches of the portal vein were larger than the common portal vein.

The left branch distal to the point of its first bifurcation was almost completely filled with large mottled red and yellow thrombus. This thrombus was not very firmly adherent to the wall of the vein. It did not appear to be old. One of its branches extended back to the main portal vein, the other extended down to the radicle which passed the quadrate lobe.

The right main branch, a few centimeters distal to the bifurcation, was markedly dilated and somewhat irregularly saccular. The walls of this vessel were calcified. It was occupied by a dark red elongated thrombus which extended into the smaller radicles distally. All of these thrombi were estimated to be 10 days old.

The hepatic artery was found to arise from the superior mesenteric artery. In tracing the artery to the liver it was found to be enlarged and very tortuous, entering the liver in about normal relationship to the common duct at the hepatoduodenal ligament.

The most startling feature of this anomalous condition of the vessels was that the tortuous hepatic artery was traced up to the saccular and calcified area in the right portal vein. At this point the artery was found to be in direct communication with the vein by a small orifice about 2 mm. in diameter. This saccular dilation appeared to be multiloculated with definitely calcified septations. No further trace nor branches of the hepatic artery could be found. Although serial sectioning of the left lobe of the liver showed small arteries in the portal spaces none of these could be traced out to their point of origin.

Varices were clearly visible in the esophagus and there were three minute ulcerations in the distal one-half of the esophagus.

The mesentery and walls of the entire intestinal tract were markedly edematous.

The right kidney weighed 188 Gm., the left 175 Gm. The left kidney had three small, thin-walled, purulent cysts on the external surface and several pitted scars.

Microscopic sections of the liver presented no significant findings except that one small vein showed organized hyaline thrombus. The left branch of the portal vein as it entered the liver contained a fairly fresh thrombus with only the earliest evidences of organization. The kidneys revealed marked degenerative disease of the proximal convoluted tubules.

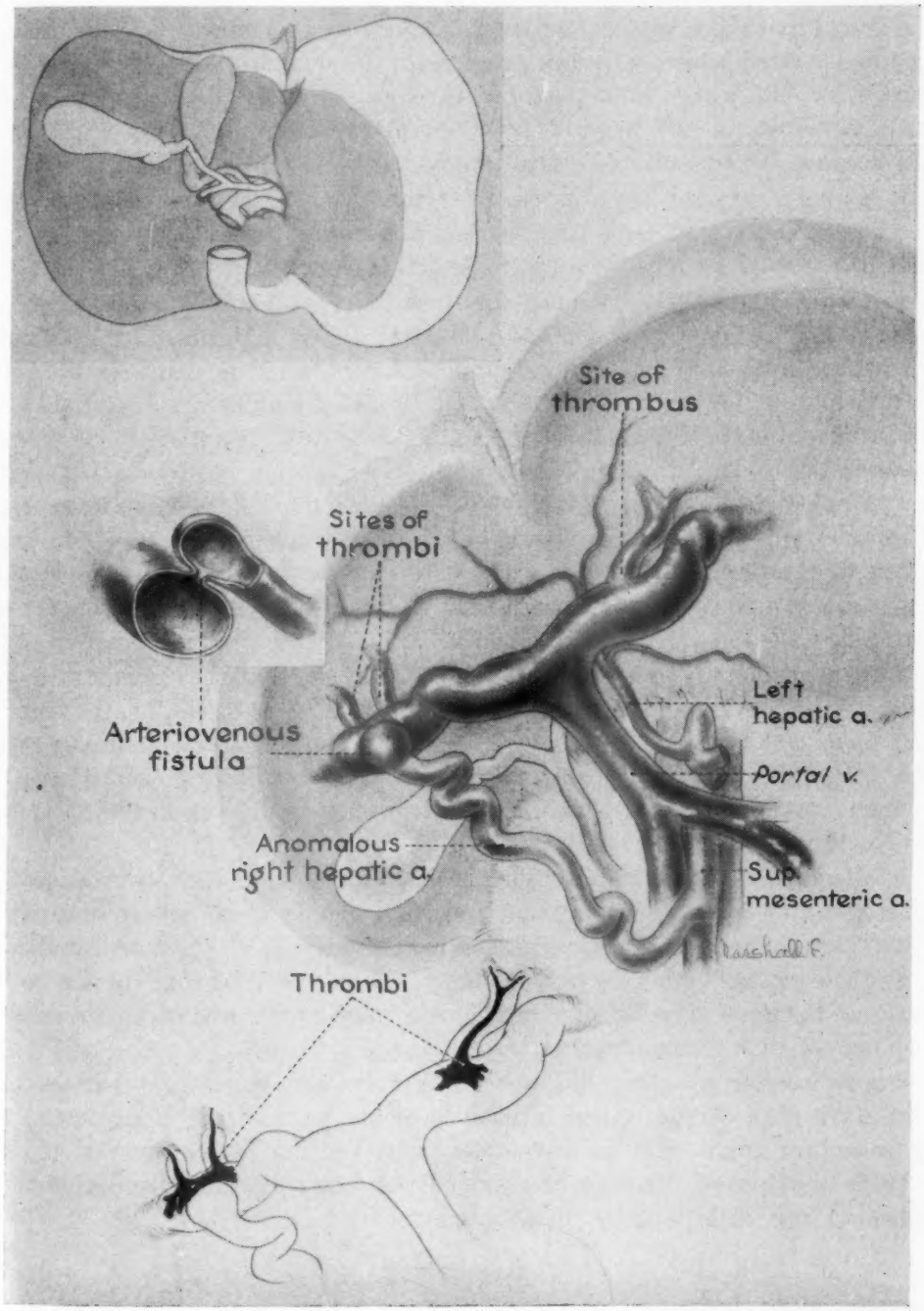


Fig. 1.—Schematic representation of autopsy findings in case of hepatic portal arteriovenous fistula (under surface liver). Insert upper left demonstrates normal liver structures in gray overlay for comparison.

DISCUSSION

Certain speculations regarding the chain of events taking place in this patient seem justified.

First of all, since considerable congential anomaly existed as indicated by the small size of the right lobe of the liver and the anomalous blood supply, one might justify the assumption that a congenital aneurysm of the hepatic artery had existed which, as years progressed, developed atherosclerotic plaques within it, one of which finally eroded through into the adjacent portal vein, thereby establishing the hepatic artery-portal vein shunt. This explanation might account for the clinical picture of portal hypertension.

It may be recalled that the initial symptoms five months prior to death were those of recurring and disappearing abdominal distention. At that time esophageal varices were not demonstrable though ascites was present.

It seems difficult to attribute the formation of ascites to portal hypertension alone, incident to hepatoportal shunt, since experimental production of such shunts by Schilling, McKee, and Wilt[17, 18] failed to demonstrate portal hypertension. Likewise, the conclusions of Volwiler, Bollman, and Grindlay[21, 22] leave little doubt that the essential factor of ascites formation is obstruction further in the liver or in the distal end of the superior vena cava. The data from pathologic examination of this case indicate that the only obstruction of the hepatic veins within the liver was apparently of not over ten days' duration. We are therefore left without an adequate explanation for the ascites which was present in this case several months prior to the development of hepatic vein obstruction.

Had a portacaval or splenorenal shunt been done at the time it had been considered in this case, an arteriovenous fistula so close to the heart would no doubt have resulted in a rapid cardiac failure since the arteriovenous fistula which initially was on the distal side of the liver capillaries would have had its effect transferred directly around the liver thereby having lost the damping effect in the liver capillary bed.

We believe that the large esophageal clot found at surgery was at least in part responsible for the prolongation and continuance of the severe hemorrhage in that it probably acted as does a clot on the surface of the tonsil bed when there is hemorrhage following tonsillectomy. It may well be that suction or Gelfoam and Patton[14] type balloon tamponade might have served to prevent development of such a nonadherent clot.

Since further bleeding did not occur from the esophageal varices after devascularization of the upper two-thirds of the stomach, it is suggested that this procedure might offer an advantage in preventing the recurrence of bleeding from that source. It may be assumed that the collateral circulation to the esophageal varices is thereby interrupted.

REFERENCES

1. Berman, J. K., Koenig, H., and Saint, W. K.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension, Quart. Bull. Indiana Univ. M. Center 12: 99, 1951.

2. Blakemore, A. H., and Lord, J. W., Jr.: The Technic of Using Vitallium Tubes in Establishing Portacaval Shunts for Portal Hypertension, Ann. Surg. **122**: 476, 1945.
3. Blakemore, A. H.: The Portacaval Shunt in the Surgical Treatment of Portal Hypertension, Ann. Surg. **128**: 825, 1948.
4. Blakemore, A. H.: Portacaval Shunt for Portal Hypertension. Follow Up Results in Cases of Cirrhosis of the Liver, J. A. M. A. **145**: 1335, 1951.
5. Blalock, A.: The Use of Shunt or By-Pass Operations in the Treatment of Certain Circulatory Disorders, Including Portal Hypertension and Pulmonic Stenosis, Ann. Surg. **125**: 129, 1947.
6. Boyce, F. F.: The Rôle of the Liver in Surgery, Springfield, Ill., 1941, Charles C Thomas, Publisher.
7. Dumais, A. F.: Vascular Studies of the Liver; M. S. Theses, Univ. of Minn. 1944.
8. Gerbode, F., Yee, J., and Rundle, F. F.: Experimental Anastomosis of Vessels to the Heart. Possible Application to Superior Vena Caval Obstruction, SURGERY **25**: 556-565, 1949.
9. Herrick, F. C.: An Experimental Study Into the Cause of Increased Portal Pressure in Portal Cirrhosis, J. Exper. Med. **9**: 93, 1907.
10. Kunkel, H. G., and Eisenmenger, W. J.: Increased Portal Pressure and Ascites in Rats Following Ligation of Portal Vein, Proc. Soc. Exper. Biol. & Med. **71**: 212, 1949.
11. Linton, R. R., Hardy, I. B., Jr., and Volwiler, W.: Portacaval Shunts in the Treatment of Portal Hypertension, Surg., Gynec. & Obst. **87**: 129, 1948.
12. Linton, R. R.: The Surgical Treatment of Bleeding Esophageal Varices by Portal Systemic Venous Shunts with a Report of 34 cases, Ann. Int. Med. **31**: 794, 1949.
13. Markowitz, J., and Rappaport, A. M.: The Hepatic Artery, Physiol. Rev. **31**: 188-204, 1951.
14. Patton, T. B., and Johnston, C. G.: A Method for Control of Bleeding From Esophageal Varices, Arch. Surg. **59**: 502, 1949.
15. Prinzmetal, M., Trnitz, E. M., Jr., Simkin, B., and Bergman, H. C.: Arterio-Venous Anastomoses in Liver, Spleen, and Lungs, Am. J. Physiol. **152**: 48-52, 1948.
16. Rousselot, L. M.: The Late Phase of Congestive Splenomegaly (Banti's Syndrome) With Hematemesis but Without Cirrhosis of the Liver, SURGERY **8**: 34-42, 1940.
17. Schilling, J. A., McKee, F. W., and Wilt, W.: Experimental Hepatic-Portal Arteriovenous Fistulae. A Report to the American College of Surgeons, Chicago, 1949.
18. Schilling, J. A., and McKee, F. W.: Experimental Hepatic-Portal Arteriovenous Anastomosis, Surg., Gynec. & Obst. **90**: 473, 1950.
19. Seneviratne, R. D.: Physiological and Pathological Responses in Blood Vessels of Liver, Quart. J. Exper. Physiol. **35**: 77-110, 1949.
20. Snell, A. M.: Discussion of Symposium on Hepatic Circulation, Proc. Staff Meet. Mayo Clin. **25**: 36, 1950.
21. Volwiler, W., Bollman, J. L., and Grindlay, J. H.: A Comparison on Two Types of Experimental Ascites, Proc. Staff Meet. Mayo Clin. **25**: 31, 1950.
22. Volwiler, W., Grindlay, H. J., and Bollman, J. L.: The Relation of Portal Vein Pressure to the Formation of Ascites; An Experimental Study. Gastroenterology **14**: 40, 1950.
23. Wakin, K. G., and Mann, F. C.: The Intrahepatic Circulation of Blood, Anat. Rec. **82**: 233-253, 1942.
24. Wangensteen, O. H.: The Ulcer Problem (Listerian Oration), Canad. M. A. J. **53**: 309, 1945.
25. Whipple, A. O.: The Problem of Portal Hypertension in Relation to Hepatosplenopathies, Ann. Surg. **122**: 449, 1945.

HOMOGENOUS SKIN GRAFTS WITH AND WITHOUT ADRENOCORTICOTROPIC HORMONES

HANS MAY, M.D., RICHARD S. OAKEY, JR., M.D., AND
GEORGE P. PILLING, IV, M.D.
PHILADELPHIA, PA.

IT IS now well established that the primary take of homogenous skin grafts is as satisfactory as that of autogenous grafts. However, the survival of this type of graft varies from a few weeks to a number of months—an exception arising in cases of identical twins (Bauer, Brown) where permanent survival is reported.

At one time it was thought that the proper selection of blood groups would improve the take of homogenous grafts, a belief which subsequent research has thus far failed to substantiate (Loeffler). Indeed, it now appears that phenomena responsible for the inability of homogenous grafts to become an organic unit with the host result from an immunologic reaction with a formation of antigens and antibodies, which cause absorption of the homografts. Medawar investigated the possibility of skin transplantation groups in rabbits and found at least 127 groups. Longmire and Smith, applying this data to man, found that there would have to be no less than 23 such groups.

After the introduction of adrenocorticotropic hormones it was thought possible to block or at least to lower the antigen antibody response of the skin and make homogenous skin transplantations permanently possible. An article has been published recently by Whitelaw, according to which homogenous pinch grafts were used from two donors to completely denuded areas of the right leg and adrenocorticotropic hormones were used. Within 58 days the grafts had not only taken but had grown to epithelize the entire area.

Homogenous grafts are used primarily today when the patient's general condition is so poor that a lengthy surgical procedure might endanger his life and when there is no sign of subcutaneous epithelization. They are also employed when the patient lacks sufficient skin of his own for complete coverage, as sometimes occurs with children. In such cases homogenous grafts are used as a physiologic dressing. During the survival of this dressing a patient's condition may be improved by supportive therapy to overcome generalized debilitation. Moreover, during this period no ordinary dressing is required; thus the patient is given a respite from the pain and exhaustion which accompanies dressing changes. Simultaneously, there is a stimulation to the patient's own epithelization, and complete healing may occur even after absorption of the homografts.

We wish to present two cases of homogenous skin grafts. In the first case large sheets of homogenous grafts were used without the use of ACTH. In the second case ACTH was used.

Received for publication, Aug. 3, 1951.

CASE 1.—The patient was a 4-year-old boy with severe third degree burns of both lower extremities (the feet excepted), both groins, the lower abdomen, the perineum and buttocks, and the lower part of the back. He was referred to our Service four months after the accident, and up to this time no local treatment had been given. The patient's condition was quite impaired, but in spite of general debilitation the granulations appeared to be in excellent condition. On the day of admission the hemoglobin was 7.5 Gm. and red blood count 3,740,000. Several blood transfusions were given, and within 10 days the patient's general condition had improved. Spit-skin grafts were then removed from his own body and used to cover the ankle and Achilles regions, plus calf and shin bones. The grafts took extremely well, roughly about 90 per cent. One week later both knee joint areas and popliteal spaces were grafted. These grafts also healed in place well (Fig. 1, *A*). However, the patient's general condition again started to slip; donor areas broke down and did not heal. Hence, we decided to resort to homografting, which was performed about three weeks later. Large sheets of grafts were used from the father to cover all raw areas (Fig. 1, *B*). The first dressing was changed one week after this operation at which time the homografts had taken well. They remained stable for about eight weeks and then showed signs of breakdown (Fig. 1, *C*). The breakdown, though, was very gradual. Meanwhile the patient's general condition had picked up markedly. There were signs of epithelization everywhere, and some of the donor areas had healed over completely (Fig. 1, *D*). About 10 weeks after the homografting, autogenous grafts were used to cover some of the raw surfaces in places where homografts had broken down. Following a lapse of three more weeks, additional autogenous grafts were used to close some of the remaining raw areas, followed by three more operations to complete the resurfacing (Fig. 1, *E*).

Microscopic examinations of the biopsies taken from the homografted areas at various intervals revealed some of the homografts still firmly intact eight weeks after the operation (Fig. 2, *A*). In some homografted areas a breakdown never occurred but biopsies taken from these areas showed no epithelial covering other than cicatricial tissue (Fig. 2, *B* and *C*). In other words, the homografts had gradually been eliminated by scar tissue which had developed between the homograft and subcutaneous tissue. There was no evidence of survival of any of the homografts. In those areas in which the homografts had been replaced by scar tissue, contractures occurred, as for instance in both groins (patient was unable to spread the legs). These contractures were not repaired immediately. The patient was sent home to allow a complete recovery, but about a year after his original admission he was readmitted and all contractures were overcome by excision of the contracted scar and application of autogenous skin grafts.

CASE 2.—The patient was a 9-year-old girl who was admitted to the hospital shortly after suffering a fire burn when her dress caught fire. The estimated burned area was 55 to 60 per cent, mostly deep. After the usual thorough cleansing of the burned area and the application of a pressure dressing, whole blood transfusion as well as plasma was administered. The second day after admission cortisone was started for adrenal replacement therapy. An initial dose of 300 mg. was given followed by 200 mg. next day, and 100 mg. each day thereafter for a total of five days' therapy. Blood and plasma transfusions were continued. The patient also was given physiologic saline and glucose solution intravenously. Antibiotics were administered. It is interesting to note that the patient's hemoglobin never went below 13.5 Gr. except once when she went into severe shock. On the tenth day following the burn the first dressing was changed under general anesthesia with infusion in place and blood available. The buttocks, posterior parts of thighs, right side of back and upper abdomen were found to have second degree burns and were healing nicely. A heavy eschar was found all over the abdomen, anterior and lateral parts of thighs, and left arm; the epidermis of the hand came off as a glovelike cast. The patient was considerably shocked following this procedure but recovered the following day. A week later some of the eschar was excised and moist saline dressings were started. After another week the dressings were changed again. Some more of the eschar was removed and autogenous split grafts were used to cover the flexion crease of the groins and the upper anterior parts of the thighs. Again the

Fig. 1, *A* to *D*.—*A*, Four-year-old boy with severe third degree burns of both lower extremities, groins, lower abdomen, perineum, buttocks, and lower part of back. Legs and knee joints were covered with autogenous split-skin grafts in three operations. General condition of patient became poor. The donor areas did not heal. *B*, Homogenous skin grafts were used from the father to close most of the raw areas. The picture was taken two weeks after the operation. *C*, Taken six weeks after the operation, this picture shows most of the homogenous grafts still intact. *D*, Ten weeks after the transplantation of the homogenous skin grafts most of the grafts had come off, but signs of epithelization are seen everywhere. The general condition of the patient was satisfactory. Most of the donor areas are healed and could now be used again to complete resurfacing of the raw areas with autogenous skin grafts.

patient went into severe shock, necessitating immediate transfusion therapy. Her hemoglobin became less than 7.5, and not enough blood was available for taking the hematocrit level.

Because of this severe reaction it was decided to use homogenous grafts to close all raw surfaces (Fig. 3, *A*). Grafts were taken from the mother the following week and applied to the girl. Inspection of the autogenous grafts at that time revealed perfect take of the grafts. ACTH therapy, 10 mg. every 6 hours, was started at this time. Two weeks later the first dressing was changed at which time all grafts were found in excellent condition. There was about 90 per cent take of the homografts, and the autografts looked firm and well healed. All homografts still were in place 4 weeks after they had been transplanted. Some, however, appeared loose, whiter, and less vascular. Microscopic examination revealed fibrinoid degeneration and partial autolysis of the graft, while the autogenous graft looked normal both microscopically and grossly. Five weeks after homografting, the homografts appeared much whiter and there were large areas of sloughing. Microscopic examination showed almost a general autolysis of the grafts. Six weeks after the homografting there was frank loss

Fig. 1,*E*.—One year after the last operation.

of all homografts, with much infection and sloughing (Fig. 3, *B*). Normal saline solution dressings were applied and in the seventh week the infection was controlled. In the eighth week the granulations looked healthy; there was no sloughing and no evidence of infection. In the midst of the granulating area which previously had been covered by homografts a fairly large skin island, measuring 3 by 4 cm., was visible. A biopsy taken from this skin island revealed normal, stable epithelium. The patient's general condition in the meantime had improved markedly. It was decided to cover all remaining raw areas with autogenous grafts, which was done 3 days later.

A question now arises: What was the origin of the skin island found in the midst of the granulations which were covered by the homogenous grafts? There is no doubt that this island was not present at the time of the homografting. After the homografts had sloughed off, the island became visible. It was fairly thin but consisted of normal epithelium. Was this island a surviving homograft or was it epithelization from the patient? It is common knowledge that with patients who have large granulating surfaces which for some reason or other are not covered by skin grafts, no epithelization will occur for weeks and weeks.

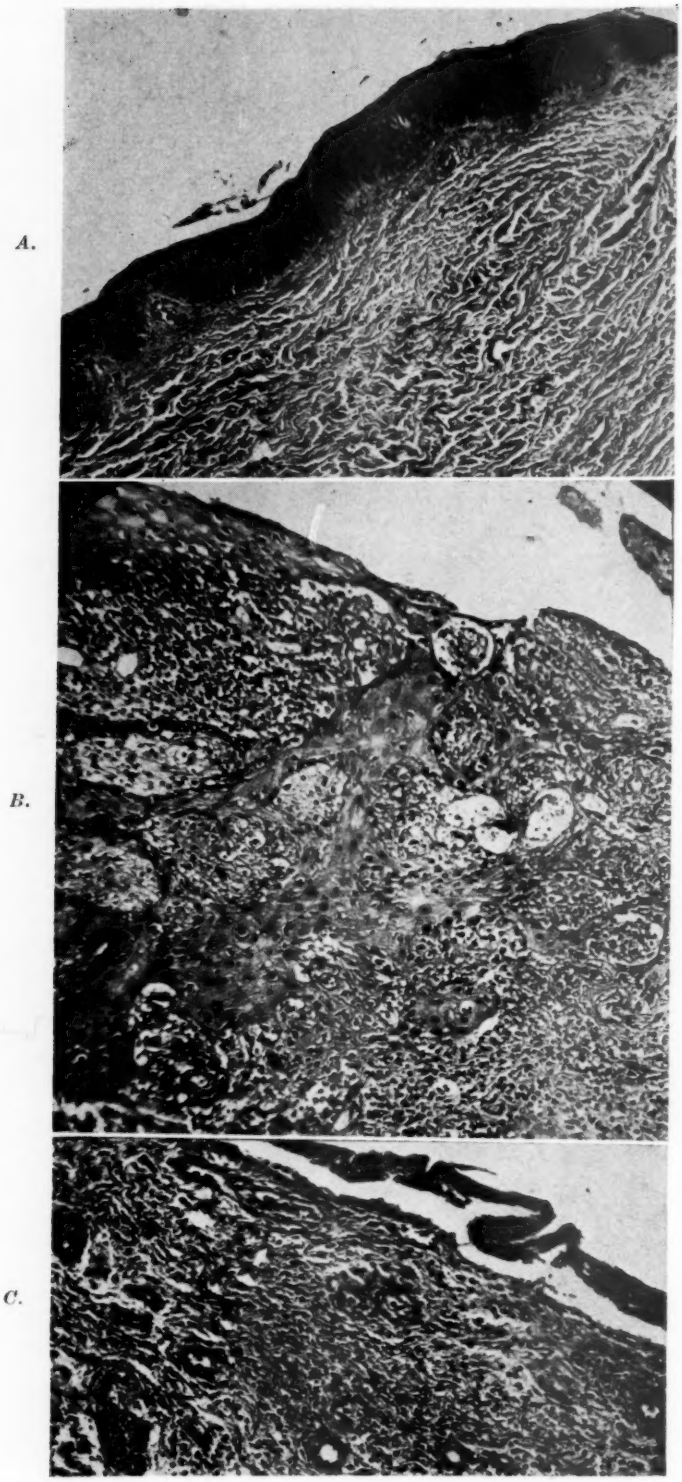


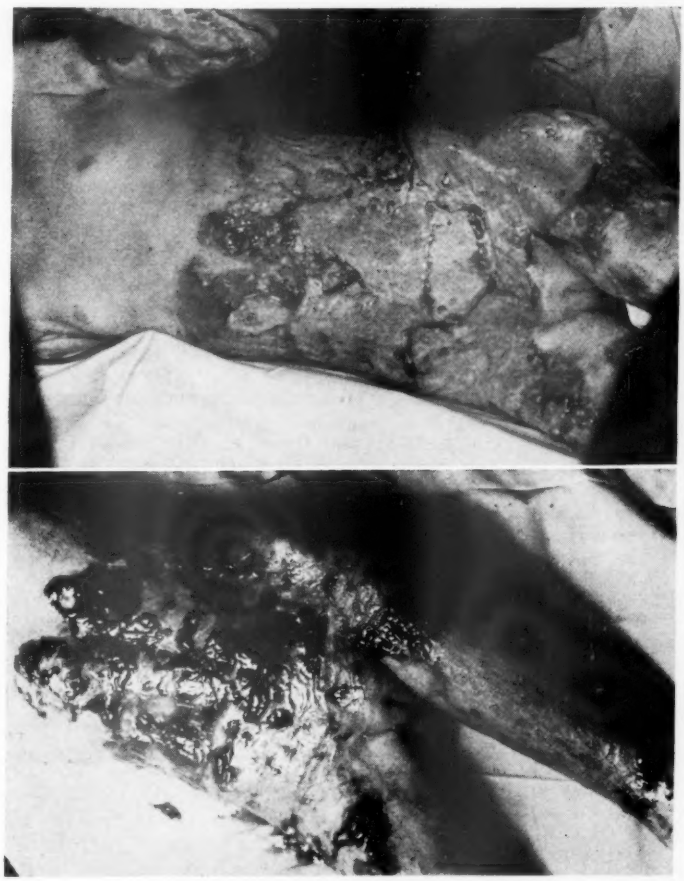
Fig. 2.—Microscopic pictures of the homogenous skin grafts of the patient depicted in Fig. 1. *A*, Skin transplanted from father six weeks after the operation. Section shows intact homologous epidermis apparently firmly united to underlying corium and subcutaneous tissue. No cellular reaction is present in the latter. *B*, and *C*, Eight weeks after the homogenous skin transplantation; these sections were taken through areas of the homogenous grafts. Both sections were taken from areas which looked intact macroscopically.

B, shows extensive exudate of lymphopolynuclear cells and fibrin in the dermis. The epidermal covering is incomplete. Remaining epidermis (left upper field) vacuolization, edema, and invasion of polymorphonuclear cells; in the center of the section finger-like invasion of the dermis by the homograft is evident. *C*, Shows atrophy and sloughing off of the homograft.

Suddenly, almost overnight, skin islands will appear in the midst of granulating area; these will grow and spread. This usually coincides with improvement of the patient's general condition.

While it is possible that we are dealing with such a condition in this patient, it is impossible to determine whether or not this skin island was a surviving homograft. Two things, however, are sure: First, after all raw surfaces had been covered by the homografts,

A.



B.

Fig. 3.—*A*, Nine-year-old girl with extensive third degree burns. The part below the marking line had been previously covered with autogenous grafts. Above the marking line homogenous grafts were placed to close the remaining raw surface. This picture was taken two weeks after the homogenous transplantation. ACTH therapy was used before and after the homogenous skin grafting. *B*, The homogenous grafts remained in place for four weeks and then showed sign of breakdown. They came off six weeks after the homografting by general autolysis.

the patient's general condition improved markedly and continued to improve even after the homografts had been absorbed. Second, ACTH did not prevent the massive sloughing and absorption of the homografts. How much it helped in stabilizing the patient's general condition, we do not know, but no striking benefits were noted in comparison with the first patient.

SUMMARY

Two patients are presented in whom large sheets of homogenous skin grafts were used to cover granulating surfaces after burns. In the first patient no

ACTH was used. The homogenous grafts remained in place up to ten weeks and absorption was very gradual. During that time the patient's general condition improved considerably, and epithelization was stimulated even in places where no grafts had been used. In the second patient ACTH was used one day prior to the application of the homogenous grafts, and continued for six weeks postoperatively. The grafts started to come off in the fifth postoperative week. Elimination and absorption was massive with much sloughing, and only one questionable island of skin remained, the origin of which cannot be determined.

REFERENCES

Bauer, K. H.: Homotransplantation von Epidermis bei eineiigen Zwillingen, Beitr. z. klin. Chir. **141:** 442, 1927.

Baxter, H., and Entin, M. A.: Clinical Study of the Fate of Homografts in Man. Effect of Repeated Dosage from the Same Donor and of Refrigeration on these Grafts, Am. J. Surg. **81:** 285, 1951.

Brown, J. B.: Homografting of Skin: With Report of Success in Identical Twins, SURGERY **1:** 558-563, 1937.

Brown, J. B., and McDowell, F.: Skin Grafting, 2 ed. Lippincott, Phila., 1949.

Brown, J. B., and McDowell, F.: Epithelial Healing and the Transplantation of Skin, Ann. Surg. **115:** 1166-1181, 1942.

Gibson, T., and Medawar, P. B.: The Fate of Skin Homografts in Man, J. Anat. **77:** 299-308, 1943.

Loeffler, C.: Die Auto- und Homo-platische Epidermis Implantation, Deutsche Ztschr. f. Chir. **236:** 169, 1932.

Longmire, W. P., Stone, H. B., Daniel, A. S., and Goon, C. D.: Report of Clinical Experience With Homografts, Plast. & Reconstruct. Surg. **2:** 419-426, 1947.

Longmire, W. P., and Smith, S. W.: Homologous Transplantation of Tissues. Arch. Surg. **62:** 443, 1951.

Medawar, P. B.: Immunity to Homologous Grafted Skin, I. The Suppression of Cell Division in Grafts Transplanted to Immunized Animals, Brit. J. Exper. Path. **27:** 9-14, 1946. II. The Relationship Between the Antigens of Blood and Skin, Brit. J. Exper. Path. **27:** 15-24, 1946.

Whitelaw, M. J.: Physiologic Reaction of ACTH in Severe Burns, J. A. M. A. **145:** 85, 1951.

UNDESIRABLE SEQUELA OF NONABSORBABLE SUTURE AS CYSTIC DUCT LIGATURE

J. HARVEY JOHNSTON, JR., M.D.,* JACKSON, MISS.

THE constant use of cotton sutures and ligatures in all types of general and thoracic surgery during the last ten years leaves no doubt in my mind that it is an unexcelled suture material. One cannot help but be impressed by the minimal tissue reaction resulting in painless, dry wounds with such excellent healing that evisceration, wound dehiscence, and incisional hernia are rarities.

The following cases make one seriously question the use of cotton or any nonabsorbable suture in ligating the cystic duct.

CASE 1.—Mrs. L. C. presented a stone in the lower end of the common duct when delayed cholangiography was done 10 days after cholecystectomy and exploration of the common duct (for chronic calculous cholecystitis and choledocholithiasis). Several attempts were made to dissolve the stone or precipitate its passage by the use of ether-alcohol mixtures (Pribram method), but were completely unsuccessful. An episode identical with acute pancreatitis developed on one occasion after instillation of ether and alcohol into the choledochus. Four weeks later the common duct was re-explored and the offending stone removed. A single No. 24 cotton ligature floated out of the common duct as bile escaped through the choledochotomy.

Postoperative Diagnosis.—(1) Choledocholithiasis, (2) foreign body (No. 24 cotton ligature) in common duct.

CASE 2.—Mrs. T. R. had cholecystectomy with exploration of the common duct elsewhere for calculous gall bladder disease. Three months later she was mildly icteric, running a low-grade fever, and having intermittent episodes of severe right upper quadrant pain.

At operation a firm granulomatous mass, about 3 cm. in diameter, was found in the region of the cystic duct. This mass was inflammatory in nature and was apparently producing extrinsic compression of the common hepatic duct. Exploration of the common duct disclosed two cotton sutures within its lumen. There was no evidence of common duct calculus; the sphincter was dilated to 9 mm. with ease.

Postoperative Diagnosis.—(1) Partial obstruction of common hepatic duct due to extrinsic inflammatory mass, (2) cotton sutures within the common duct.

CASE 3.—Mr. D. W. had cholecystectomy without choledochostomy at another hospital for chronic calculous cholecystitis of long standing. A subdiaphragmatic abscess requiring drainage developed postoperatively. He continued to have low-grade jaundice, mild fever, and intermittent, colicky right upper quadrant pain, which the patient described as being identical to his preoperative seizures.

Surgical exploration disclosed a dilated common duct containing three large, soft stones, one of which was impacted at the sphincter of Oddi. In exploring the common duct a free ligature of No. 30 cotton was found within the lumen of the duct. The knot of a transfixion suture of cotton, which was still attached to the cystic duct stump, had eroded through the wall of the common duct and presented within its lumen (Fig. 1).

Postoperative Diagnosis.—(1) Common duct obstruction due to choledocholithiasis, (2) nonabsorbable sutures in lumen of common duct.

Received for publication, Aug. 10, 1951.
*Chief, Surgical Section, Mississippi Baptist Hospital.

DISCUSSION

In none of the cases presented were the foreign bodies found within the common duct the essential pathology. All of the clinical symptoms could be adequately explained by the common duct stones found in Cases 1 and 3, and by the extrinsic inflammatory mass found in Case 2. There can be little doubt that nonabsorbable sutures can persist in the common duct for long periods of time without symptoms, or can pass through the sphincter of Oddi without difficulty. There is no question, however, that such foreign bodies within the duct are undesirable and could easily serve as a nidus for stone formation or continued infection within the common duct.

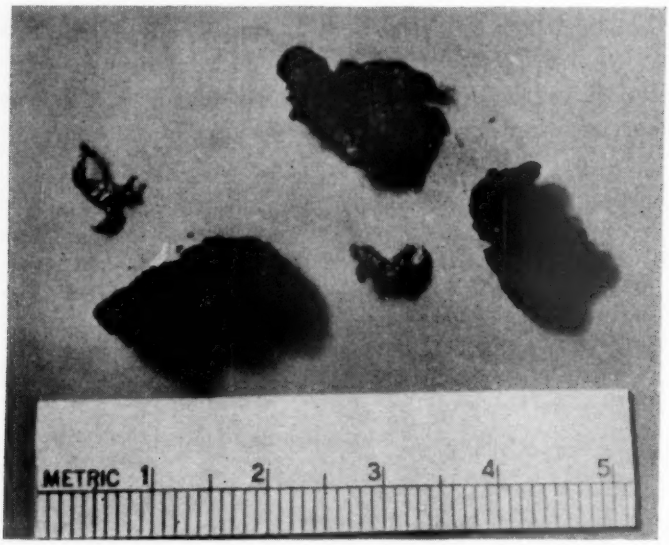


Fig. 1.—Three soft stones and two No. 30 cotton ligatures removed from common duct in Case 3.

CONCLUSION

On the basis of the three reported cases in which nonabsorbable sutures used in ligating the cystic duct had eroded through the wall of the common duct and were present within the extrahepatic biliary system, it is suggested that the use of such sutures in ligating the cystic duct be discontinued, for adequate closure of the cystic duct can be accomplished with a ligature and transfixion suture of small chromic catgut. Peritonealization after gall bladder surgery usually places the cystic duct in immediate apposition to the common or hepatic bile ducts, so that erosion of a nonabsorbable suture from the ligated cystic duct into the common duct no doubt occurs more frequently than has been realized.

RECURRENT GALLSTONE ILEUS

A Case Report

EUGENE A. NOSKIN, B.S., M.D.,* AND WILLIAM J. TANNENBAUM, M.D.,**
CHICAGO, ILL.

THIS report is presented because we feel that it is interesting, and to add another case to the literature on recurrent gallstone ileus.

In 1929 Holz[1] listed five cases in which gallstone obstruction had occurred in the same individual more than once; in three of these the second stone was removed during the immediate convalescence from the first operation. Included in this group was the case listed by Pybus.[2] Following this report, Downes[3] added another case; another one was added by Schwarke in 1938.[4] The eighth case was reported by Hinchey in 1940.[5] Again, in 1943, a case was added by Hand and Gilmore[6] to bring the total to nine. We wish at this time to add the tenth case to the literature on recurrent gallstone obstruction or ileus.

CASE REPORT

A 69-year-old housewife was admitted to Michael Reese Hospital on Dec. 2, 1948, complaining of vomiting accompanied by abdominal cramps of six days' duration. She claimed that she had experienced similar cramps two years previously. Following the onset of her symptoms she had normal bowel movements for two days and from that time until admission had no more movements. For the twenty-four hours prior to admission she had passed no gas and had urinated only scanty amounts. There had been no weight loss.

Physical examination revealed a well-developed, well-nourished white woman in no apparent distress. Her blood pressure was 134/60 mm. Hg, temperature 98.6° F., respirations 20, pulse 92. There was a slight loss of tissue turgor. Physical examination was otherwise essentially normal except for moderate diffuse tenderness throughout the entire abdomen. Bowel sounds were present and normal. Rectal examination revealed a few hemorrhoidal tags and soft stool (normal in color) on the examining finger.

On admission red blood count was 5.6 million per cubic centimeter, white blood count 9,406 per cubic centimeter, hemoglobin 18.1 Gm., hematocrit 52, sedimentation rate 18 mm. per hour. Differential smear showed polymorphonuclears 75 per cent, lymphocytes 20 per cent, monocytes 5 per cent. Urinalysis showed a specific gravity of 1.017, albumin 2 plus. On microscopic examination of the sediment there were a few red blood cells and five to ten white blood cells. The Kahn test was negative. The stool was positive for blood by the benzidine and guaiac tests. Serum glucose was 132 mg. per cent and the serum urea nitrogen was 145 mg. per cent.

Due to the fact that the patient had an elevated blood urea nitrogen and the fact that the abdominal symptoms subsided, she was treated conservatively. However, on the fourth day after admission the abdomen again became distended and the abdominal cramps recurred. At this time peristaltic rushes were heard. The abdomen became tender, especially in the left lower quadrant. A scout film of the abdomen at this time revealed dilated loops of small intestine and two calcific shadows in the region of the gall bladder (Fig. 1). She was placed on intestinal intubation with suction and an exploratory laparotomy was decided upon.

Under general anesthesia the abdomen was opened through a lower right paramedian incision. The jejunum and ileum were dilated to a point about 30 cm. from the ileocecal valve. Beyond this point the ileum was contracted. At this point, however, a lime-sized mass was palpated. The lumen was entered in the direction of the long axis of the small

Received for publication, Aug. 13, 1951.

*Formerly Chief Surgical Resident, Michael Reese Hospital.
**Associate Surgeon, Michael Reese Hospital.

Fig. 1.

Fig. 2.

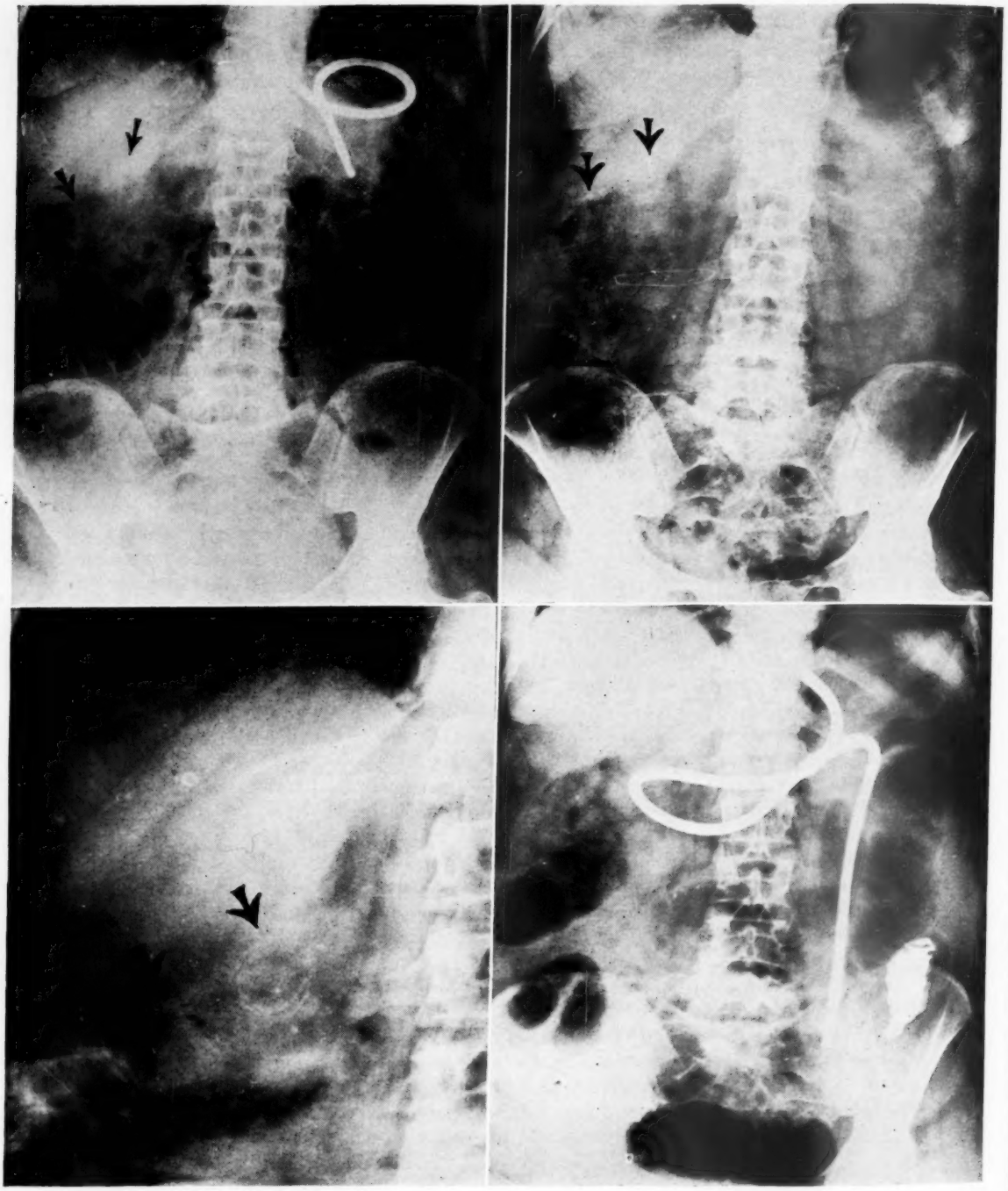


Fig. 3.

Fig. 4.

Fig. 1.—Note two radiopaque shadows in right upper quadrant and loops of distended small intestine.

Fig. 2.—Note radiopaque shadows still present postoperatively, small intestinal distention absent. (Film taken during convalescence.)

Fig. 3.—Five months postoperative cholecystogram shows nonfunctioning gall bladder with presence of two radiopaque shadows.

Fig. 4.—Note small intestinal distention. Radiopaque shadows are absent.

intestine and a large gallstone removed. This was accompanied by a large amount of liquid intestinal content. The ileum was then closed transversely. The abdomen was then closed in the usual fashion in layers. The patient was returned to her room in good condition. Within twenty-four hours the patient was passing gas and a small amount of stool.

Postoperatively she developed an extrarenal azotemia, a suppurative wound infection, and a large incisional hernia. Following a very stormy postoperative course she was discharged on the forty-fourth day (Fig. 2).

A cholecystogram five months later showed two large stones in the gall bladder, but the gall bladder did not concentrate the dye (Fig. 3).

Thirteen months following her first admission, she was again admitted to the hospital complaining of colicky abdominal pain and vomiting of five days' duration. The vomitus had a feculent odor. The bowels had not been moved for five days. Physical examination showed that the patient had all the signs of dehydration. The blood pressure was 145/65 mm. Hg. The abdomen was markedly distended and through the hernial defect peristaltic waves were visible. Bowel sounds were hyperactive and peristaltic rushes could be heard. A scout film of the abdomen showed gaseous distention of the small intestine down to the middle of the ileum.

The patient was placed on intestinal intubation (Cantor tube) in preparation for surgery and within two hours the tube was in the duodenum as evidenced by the return of golden bile (Fig. 4). The abdomen became soft and the return from the suction tube became fecal in character. At about this time a mass about the size of a golf ball was palpated through the hernial defect in the right lower quadrant. The laparotomy was then performed with the preoperative diagnosis of recurrent gallstone ileus.

When the abdomen was entered through the old incisional scar numerous loops of dilated small intestine were found to be present, filling the hernial sac. The dilated loops were traced down to a point about 30 cm. from the ileocecal valve, and at this point the ileum was bound down to the abdominal wall by a fibrous adhesion. Just proximal to this point a hard mass was palpated within the lumen of the ileum. An enterotomy was performed and a golf ball-sized gallstone was removed from the ileum as was a large amount of liquid intestinal content. The ileum was then closed transversely and the abdomen was closed in two layers. The postoperative course was uneventful except for a subcutaneous wound infection. The patient was discharged on the nineteenth postoperative day. A repeat cholecystogram showed no further calcified masses, although the gall bladder did not concentrate the dye. At the time of discharge she was advised to return for cholecystectomy at a later date. She has, however, left Chicago and further contact is impossible.

CONCLUSION

We have presented a case of recurrent gallstone ileus, as an interesting case and the tenth to be reported in the literature. As no fistula was demonstrated on x-ray examination we can only postulate that a cholecystenteric fistula (cholecystoduodenal) exists.

We can also conclude that the recurrence of the intestinal obstruction would not have occurred had a cholecystectomy been performed after her first operation.

REFERENCES

1. Holz, E.: Quoted by Hinchey.[5]
2. Pybus, F. C.: A Note on Two Cases of Gallstone Ileus, Lancet 2: 812, 1922.
3. Downes, W. A.: Discussion of Moschowitz, Ann. Surg. 61: 243-244, 1915.
4. Schwarke, R.: Quoted by Hinchey.[5]
5. Hinchey, P. R.: Recurrent Gallstone Ileus, New England J. Med. 223: 174-179, 1940.
6. Hand, B. H., and Gilmore, W. E.: Gallstone Ileus, Am. J. Surg. 59: 72-78, 1943.

THE FATE OF THE INCISED COMMISSURE IN MITRAL STENOSIS

Post-Mortem Findings in Two Cases

William H. Muller, Jr., M.D.,* Los Angeles, Calif.

ALTHOUGH in most of the early surgical procedures designed for the relief of mitral stenosis a portion of one of the valve leaflets was excised,[1, 2] incision or tearing of the valve ring in the region of the commissure is the method most frequently used at present.

In the development of mitral commissurotomy, one of the objections to simple incision of the commissures has been the possibility that the ring might heal together at the site of the incisions. This report is a presentation of the findings from the post-mortem examination of the hearts of two patients who were treated for mitral stenosis by commissurotomy. One of them died three weeks and one seven months after operation.

CASE HISTORIES

Case 1.—This 29-year-old white woman was admitted to the Los Angeles County Harbor General Hospital on May 15, 1950. She had had rheumatic fever at the age of 11 years. No cardiac symptoms were present until she began to have increasing fatigability and exertional dyspnea about nine years prior to her admission for commissurotomy. These symptoms progressed rapidly until she was having numerous episodes of pulmonary edema, hemoptysis, and right ventricular failure. She had required digitalis for several years, and quinidine had been necessary to convert an episode of auricular fibrillation. Mercurial diuretics two or three times a week were necessary also. Hospital admission to control her heart failure was required on two occasions during the four months preceding her admission for operation.

The patient was well developed and well nourished. She appeared her stated age, was in no acute distress, and did not appear chronically ill. The chest was symmetrical without respiratory lag. There were fine râles over both bases. A slight diastolic thrill could be felt over the apical region of the precordium. The heart was not enlarged to percussion. A long diastolic murmur was present over the apex and was transmitted to the axillary region. A less intense systolic murmur was present over the same area. The pulmonic second sound was markedly accentuated. The blood pressure was 135/85, and the venous pressure was 8 cm. of water. The abdomen was flat without masses or tenderness. The liver and spleen were not palpable. No ankle edema was present.

The red blood cell count was 4.95 million, hemoglobin 14 Gm., hematocrit 38. The white blood cell count on admission was 15,500 with an essentially normal differential count. The urinalysis was normal. The Kahn test and cephalin flocculation were negative. The prothrombin time was 14.7 seconds or 100 per cent. Total proteins were 5.68, albumin 4.11, globulin 1.57. Chlorides were 460 mg. per cent. The blood urea nitrogen ranged from 17 to 22 mg. per cent. X-ray and fluoroscopic examination showed evidence of moderate cardiac enlargement in the posteroanterior projection with straightening of the left cardiac border

---

Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Received for publication, Aug. 27, 1951.

*From the Department of Surgery, School of Medicine, University of California at Los Angeles; the Department of Surgery, Veterans Administration Center Wadsworth Hospital, Los Angeles; and the Section of Cardiovascular Surgery, Los Angeles County Harbor General Hospital, Torrance, Calif.

and a prominent pulmonary segment. A double contour shadow could be seen on the right. Oblique views showed evidence of enlargement of the right ventricle and left auricle. The main stem bronchus was elevated. The impression was rheumatic heart disease with mitral valvular involvement showing evidence of right ventricular and left auricular enlargement. The electrocardiographic findings were consistent with those of mitral stenosis. It was felt that this patient had a predominantly stenotic deformity of the mitral valve, and on May 22, 1950, a commissurotomy was performed.

The patient's immediate postoperative course was stormy. There was some atelectasis of the left lung which was relieved by tracheal aspirations. Auricular fibrillation began on the fourth postoperative day and was accompanied by tachycardia. At this time it was also noted that the right leg was slightly tender and swollen, and a diagnosis of thrombophlebitis was made. The fibrillation was converted with quinidine to a normal rhythm, and the thrombophlebitis responded to antibiotics and nonoperative treatment. The patient was allowed to be up on the tenth postoperative day and was without symptoms. She stated that she no longer had exertional dyspnea and felt much better than before her operation. On the sixteenth postoperative day a sudden pain occurred in the left side of the chest and was accompanied by an elevated temperature. She became markedly dyspneic and orthopneic and slightly cyanotic. Her pulse rate rose to 120 and bilateral basilar râles developed. In spite of all therapy her condition became progressively poorer, and she died on June 8, 1950, 18 days following her operation.

CASE 2.—This patient was a 29-year-old white man who was admitted to the Veterans Administration Center Wadsworth Hospital on Oct. 27, 1950. A diagnosis of rheumatic heart disease accompanied by mitral stenosis and mitral insufficiency was made. There was no history of rheumatic fever. He first began to have increasing fatigability and dyspnea about three years prior to admission and was first admitted to another hospital approximately six months after onset of symptoms, complaining of dyspnea, hemoptysis, and ankle edema. These symptoms responded to a medical regime, and the patient was discharged but was readmitted at intervals of approximately six months for recurrent episodes of cardiac decompensation. The episodes became progressively more frequent.

Physical examination revealed a well-developed but somewhat undernourished white man who did not appear chronically or acutely ill. The chest was symmetrical and there was no respiratory lag. The heart was enlarged to percussion. The point of maximum impulse was in the fifth intercostal space 1 cm. to the right of the anterior axillary line. A diastolic thrill could be felt in the apical region. The rhythm was that of auricular fibrillation. A low pitched, rumbling, mid-diastolic murmur and a high pitched systolic murmur were present in the mitral region. No aortic murmurs were present. The pulmonic second sound was accentuated. The blood pressure was 110/75, and the pluse rate was 50. Examination of the abdomen revealed that the liver was palpable 2 cm. below the right costal margin. Ankle edema was not present.

The red blood cell count was 5.5 million, hemoglobin 14.5 Gm. (106 per cent). The white blood cell count was 9,350 with an essentially normal differential count. The sedimentation rate was 9 mm. per hour. The blood urea nitrogen was 12 mg. per cent. The serum potassium was 17½ mg. per cent. Carbon dioxide combining power was 51 volumes per cent. Cephalin flocculation was negative. Thymol turbidity was 5.5 units, and serum bilirubin 5.7. Urinalysis and serological studies were negative. The venous pressure was 8 cm. of water. The circulation time was 40 seconds with Decholin and 16 seconds with ether. The vital capacity was 4.6 liters.

X-ray and fluoroscopic reports showed changes typical of those produced by mitral stenosis, including an enlarged right ventricle and left auricle. The calcified mitral valve could be seen. There was a prominent main pulmonary artery and pulmonary conus, and the left main stem bronchus was elevated.

Electrocardiographic examination showed incomplete right bundle branch block and auricular fibrillation. The rhythm was converted to a normal sinus rhythm following the

administration of quinidine. He was maintained on a salt-free diet and was given 1½ grains of digitalis daily. Commissurotomy was performed on Nov. 22, 1950. He was discharged from the hospital on Dec. 12, 1950, after a fairly uneventful postoperative course.

Shortly after his discharge the patient was admitted to another hospital at frequent intervals because of episodes of chest pain. This pain occurred over the left hemithorax at first but subsequently involved the right side of the chest also. Pulmonary emboli were suspected but were not proved to have occurred. He became progressively more dyspneic and began to have episodes of congestive failure. X-rays taken four months following his operation showed that the heart had increased markedly in size. This enlargement appeared to be primarily in the region of the left ventricle. On May 5, 1951, he contracted what he thought was a cold and began to have a productive cough accompanied by more severe dyspnea. His local physician diagnosed bronchitis, but his symptoms progressed and he was treated with Chloromycetin and penicillin. He was admitted to the hospital again on May 15, 1951, where he remained in cardiac failure. His failure became progressively worse and he died on June 24, 1951.

POST-MORTEM FINDINGS

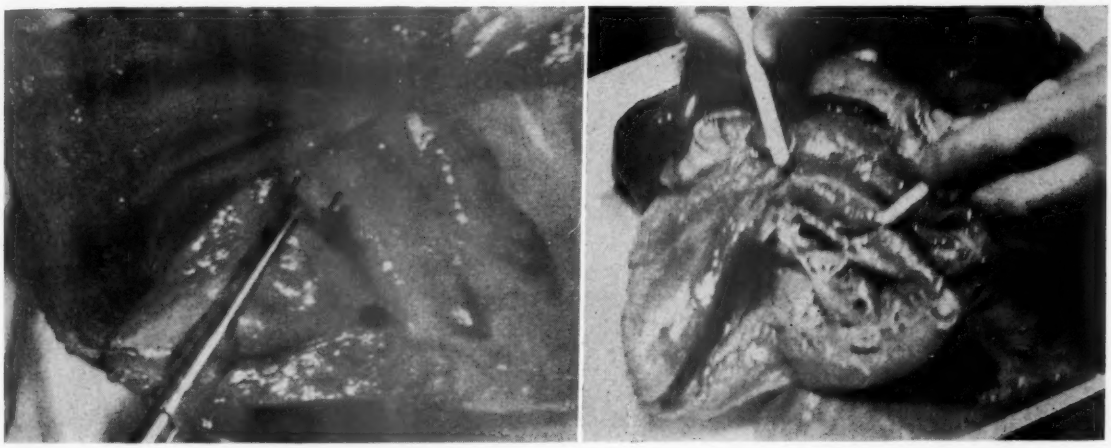
Post-mortem studies of the first patient confirmed the presence of a pulmonary infarct in the left lung. The heart showed hypertrophy of the right ventricle, an enlarged pulmonary artery and left auricle, and a partially calcified stenotic mitral valve with an incision in the lateral commissure. The valve opening would admit two fingers (Fig. 1). The incised edges appeared to be covered by endothelium, and there was no gross evidence of healing together at the point of incision. Histologic studies were not made through the area of the commissurotomy.

In the second patient, post-mortem studies revealed right ventricular hypertrophy and dilatation. The pulmonary artery, left auricle, and left ventricle were enlarged, and the mitral valve was markedly calcified except for one small area in the posterior leaflet. An incision about 10 mm. long was present in the medial commissure and one about 5 mm. long was present in the lateral commissure (Fig. 2). A tear was present in a thin portion of the lateral aspect of the posterior leaflet. There was no gross evidence of endothelization over the incised calcified surfaces. These areas were granular. There appeared to be no healing together of the borders of the incised commissures. Specimens taken from the commissures for histologic studies were decalcified. This procedure resulted in an unsatisfactory section from the heavily calcified medial commissure. On examination of the specimen taken from the lateral commissure, one could see a defect extending from the free edge through the underlying substantia spongiosa and fibrosa layers into the valve ring (Fig. 3, *A*). There was a small amount of fibrin along the incised edges but no endothelium was present. Slight vascularization and mild infiltration of lymphocytes could be seen several millimeters away from the cut edge, but no fibroblastic activity was present. Collagen in the fibrosa layer was relatively accellular (Fig. 3, *B*).

From these findings we concluded that no healing or cicatrizing process had taken place. It seems likely that endothelization probably would not occur on the cut surfaces of extremely calcified tissues. Endothelium was found both grossly and microscopically on the borders of the tear in the posterior leaflet where there was almost no calcification.

DISCUSSION

Cutler, Levine, and Beck[1] attempted to incise the posterior valve leaflet at first with a long-handled knife but subsequently developed the cardiovalvulotome which they used to excise a portion of one of the leaflets because the knife which they had used in their first three cases would not cut through a fibrotic calcareous valve. Other investigators, including Pribram[3] and Smithy and associates,[2] used similar instruments to accomplish this end. Bailey and associates[4, 5] and Harken and associates[6] were the first to suggest that the valve ring be divided in the region of the commissures so that the stenosis would be relieved,



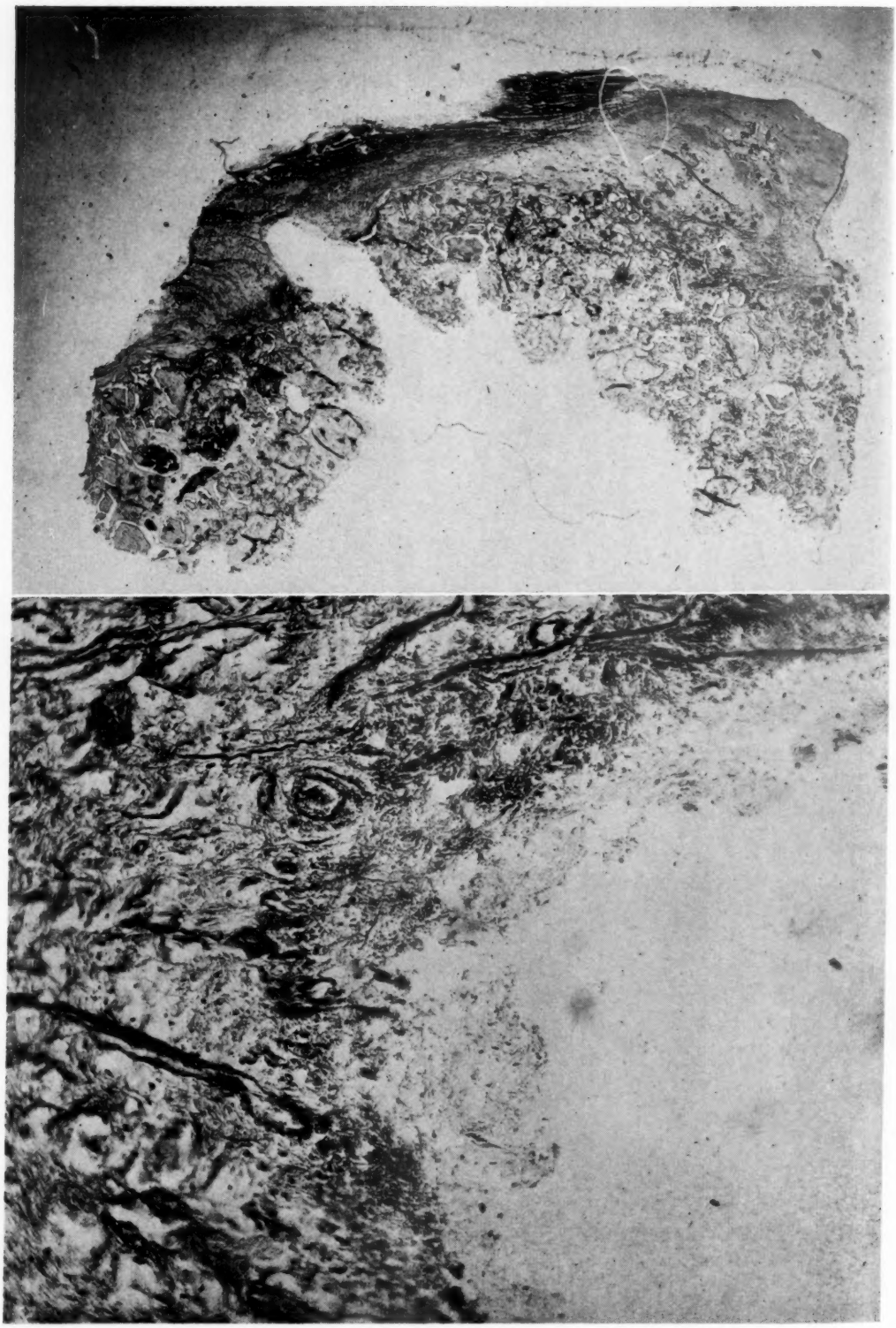
A. *B.*

Fig. 1.—*A*, Photograph of mitral valve from the first patient, taken from the auricular side. The left auricle has been removed. The arrows mark the limits of the incision in the commissure.

B, Mitral valve photographed from the ventricular side. The opening will admit two fingers.

Fig. 2.—Photograph of mitral valve from second patient. The arrows mark the extent of the incisions in both commissures. The incised surfaces of the highly calcified, rough-appearing medial commissure are granular. No vegetations or thrombi are present. The defect opposite the single arrow is a tear in the posterior leaflet. The break in the anterior leaflet occurred post mortem.

A.



B.

Fig. 3.—*A,* Low-power photomicrograph of histologic section from the heart of the second patient illustrating the incision in the lateral commissure.

B, Photomicrograph of tissue at the deepest point of the incision in the lateral commissure of the heart of the second patient. A thin layer of fibrin containing a few fibroblasts covers the cut surface. No endothelium is present.

but a minimal amount of additional insufficiency would be produced. Harken and his co-workers excised a portion of the commissures. Bailey and his associates made incisions in them. The question has often arisen among investigators who have worked on this problem as to whether or not simple incisions in the thick fibrous and often calcified mitral valve would heal together. Cutler and associates[1] state that the incised margins of the valve heal without the formation of a thrombus but that the healed margin is often thickened and rumpled. The thickening is caused by the infiltration of round cells and fibroblasts. The edges are covered with endothelium. They felt that an incision alone in the valve was inadequate to relieve the obstruction. In speaking of the incised normal valve in the dog, Allen[7] states that one would expect a certain number to have vegetation-like thrombi on the edges but that endocardium rapidly proliferates and in a short time completely covers the raw surfaces. In one dog, allowed to live eleven months, the incision still extended through the entire leaflet. Bailey, Glover, and O'Neill[4, 5] believe that it is improbable that healing will occur if the valve ring is incised to the extent that the edges will gape widely during most of the cardiac cycle. They feel, however, that if the incisions extend only partially through the ring of scar tissue, the edges can not spread apart and healing will probably occur. In their experience the incised normal valves in dogs did not heal together in the twelve months during which the animals were followed. In one of their patients who died three months after commissurotomy no healing together of the incised edges was observed.

In a recent publication, Blalock[8] points out that it is too early to evaluate the long-term benefits of the operation and that the stenosis might gradually recur. He suggests that if this is the case it might be necessary to remove a segment of the valve.

Although in our patient who was observed for seven months, no evidence of healing together for the incised commissures was found at autopsy, the possibility of the gradual reformation of mitral stenosis is not entirely excluded. When one considers that the initial stenosis probably develops in many cases over a period of several years after the onset of rheumatic heart disease, it seems entirely possible that the stenosis may recur after commissurotomy, especially when there are unrecognized bouts of rheumatic fever. However, in view of the fact that the incised calcified commissures in the second patient showed no gross or microscopic evidence of healing together even in the presence of a tear in the posterior leaflet which allowed close contact of the incised edges, it seems unlikely that healing together would subsequently occur and result in stenosis.

This case also emphasizes that extreme care must be used not to tear one of the valve leaflets when one tears the commissure with the finger.

SUMMARY

The case histories and post-mortem findings on the hearts of two patients who died at three weeks and seven months after commissurotomy for mitral stenosis are presented.

No evidence of healing together of the incised borders of the commissures could be found.

It is concluded that healing together of the incised borders of the commissures after comissurotomy probably does not occur.

Appreciation is expressed to B. G. Fishkin, M.D., for his help with the pathologic studies for this report.

REFERENCES

1. Cutler, Elliott C., Levine, Samuel A., and Beck, Claude S.: The Surgical Treatment of Mitral Stenosis: Experimental and Clinical Studies, Arch. Surg. **9**: 689, 1924.
2. Smithy, Horace G., Boone, John A., and Stallworth, J. Manly: Surgical Treatment of Constrictive Valvular Disease of the Heart, Surg., Gynec. & Obst. **90**: 175, 1950.
3. Pribram, B. O.: Die Operative Behandlung der Mitral Stenose, Arch. f. Klin. Chir. **142**: 458, 1925.
4. Bailey, Charles, Glover, Robert P., and O'Neill, Thomas J. E.: The Surgery of Mitral Stenosis, J. Thoracic Surg. **19**: 16, 1950.
5. Glover, Robert P., O'Neill, Thomas J. E., and Bailey, Charles P.: Mitral Stenosis: Its Surgical Treatment by Commissurotomy, Pennsylvania M. J. **53**: 375, 1950.
6. Harken, Dwight E., Ellis, Laurence B., Ware, Paul F., and Norman, Leona R.: The Surgical Treatment of Mitral Stenosis. I. Valvuloplasty, New England J. Med. **239**: 801, 1948.
7. Allen, Duff S.: Intracardiac Surgery, Arch. Surg. **8**: 317, 1924.
8. Blalock, Alfred: A Consideration of Some of the Problems in Cardiovascular Surgery, J. Thoracic Surg. **21**: 543, 1951.

JEJUNAL INTUSSUSCEPTION IN CHILDHOOD DUE TO TUMOR

CLARENCE J. SCHEIN, M.D., AND LEON BLUESTONE, M.D., NEW YORK, N. Y.

(From the Surgical Service of the Lincoln Hospital)

CHILDHOOD intussusception has been extensively reviewed and has come to be recognized as a relatively frequent and urgent surgical problem. The majority of these intussusceptions present in the ileocecal area and are of undetermined etiology, although frequently associated with mesenteric adenitis, enteritis, enlarged Peyer's patches and failure of cecal fixation. This case is of interest because it presents an infrequent site of intussusception in which the etiological polyp was primarly resected. We have been able to discover only five other cases of polypoid jejunojejunal intussusception occurring in early childhood.

CASE REPORT

W. R., an eight-year-old white child, was admitted to the Lincoln Hospital on June 24, 1950, for colicky abdominal pain and vomiting of twelve hours' duration. In the past few months there had been four similar episodes which had subsided spontaneously. The present illness had started abruptly. Examination revealed moderate abdominal distention and tenderness in the left upper quadrant, where a large distended loop of bowel was palpated. Rectal examination was negative. Temperature was 101° F. and white blood count 18,000 with 90 per cent polymorphonuclear leukocytes. Flat film of the abdomen revealed a localized distended loop of small bowel in the left upper quadrant. A provisional diagnosis of small intestinal obstruction due to intussusception was made.

Laparotomy was performed through a right rectus incision. The peritoneal cavity contained 200 c.c. of clear yellow fluid. A congested small bowel presented as a volvulus which had rotated two and one-half times about the axis of the mesentery. When this was detorsioned a jejunojejunal intussusception presented eight inches from the ligament of Treitz. The intussusception was reduced without difficulty and the viability of the bowel restored with hot laparotomy pads. At the head of the intussusception there was a broad-based polyp which occluded the bowel lumen for about 80 per cent of its diameter. The serosa of the jejunum was invaginated at the base of the polyp and the mesentery contained many large lymph nodes. A resection and end-to-end anastomosis were performed. The postoperative course was uneventful.

The resected specimen consisted of 34 cm. of jejunum in the center of which there was a polyp measuring 2.5 by 2 cm. in size. Microscopic examination revealed an adenomatous polyp, congestive changes in the jejunum, and hyperplasia of the mesenteric lymph nodes.

A small intestinal x-ray study done two months postoperatively showed no abnormalities. One year later the patient was asymptomatic.

DISCUSSION

The pathogenesis of this clinical picture is based upon the presence of the large adenomatous polyp which acted as the head of the intussusception. The

Received for publication, Nov. 20, 1951.

proximal loop acted to overcome this intraluminal obstruction. Torsion and volvulus resulted from continued peristalsis acting on the weighted mass of congested intussuscepted bowel.

Freilich and Coe[3] reviewed the literature to 1937 and reported jejunojejunal intussusception in 0.9 per cent of 3,284 cases. In the larger reviews of intussusception the number of enteroenteric intussusceptions has been small, constituting 5 per cent of the 610 cases reported by Gross and Ware,[6] 3 per cent of the cases reported by Hogg and Donovan,[7] 8 per cent of the cases reported by Gibbs and Sutton,[4] and 12 per cent of the cases reported by Kohle.[10] Jejunojejunal intussusception is the least frequent localization in children.

Table I presents the five cases reported in the literature occurring in children under the age of ten years in which a precipitating factor could be demonstrated.

TABLE I

AUTHOR	YEAR	AGE	PROCEDURE	RESULT	ETIOLOGY
Reisinger[13]	1930	8½ yr.	Resection	Survival	Polyp
DeTarnowsky and Sarma[1]	1934	4 mo.	Resection	Died	Papilloma
Fiske[2]	1937	10 yr.	Resection	Survival	Polyp
Kempton and Crane[9]	1938	7 yr.	Resection	Survival	Ectopic gastric mucosa
Merchant[11]	1939	8 yr.	Resection	Died	Hemangioma
Schein and Bluestone	1951	8 yr.	Resection	Survival	Polyp

This series of cases is small and it is not possible to draw statistically valid conclusions from it. However, there are several observations that seem pertinent. All of these cases required resection at the time of laparotomy, either because the viability of the bowel had already been compromised or in order to remove the etiological factor. The operative mortality is 33.3 per cent. In all cases the etiological agent is pathologically benign. This is in marked contrast to the jejunal intussusceptions encountered in adults.[5, 8, 12]

The clinical picture in these cases differs from that encountered in the usual type of ileocolic intussusception in two major respects. In contrast to the latter, these patients present an acute episode superimposed on a history suggestive of previous bouts of intermittent intussusception that have probably reduced spontaneously. Bleeding is rarely observed in the acute episode of a high intussusception. Intestinal resection is more frequently necessary as the indicated surgical procedure.

SUMMARY

1. The sixth case of polypoid jejunojejunal intussusception is presented.

2. These cases are characterized by recurrent symptoms, infrequent acute bleeding, and the need for immediate surgical resectional therapy.

REFERENCES

1. DeTarnowsky, G., and Sarma, P. S.: Polyp of Jejunum Causing Intussusception, S. Clin. North America **14**: 879, 1934.
2. Fiske, F. A.: Intussusception Due to Intestinal Tumors, Ann. Surg. **106**: 221, 1937.
3. Freilich, E. B., and Coe, G. C.: Jejunal Intussusception, Ann. Surg. **105**: 183, 1936.

4. Gibbs, E. W., and Sutton, P. W.: Intussusception, SURGERY **14**: 78, 1943.
5. Green, N. W.: Polypoid Adenocarcinoma of the Jejunum With Intussusception, Ann. Surg. **88**: 1114, 1928.
6. Gross, R. E., and Ware, P. F.: Intussusception in Childhood, New England J. Med. **239**: 645, 1948.
7. Hogg, B. M., and Donovan, E. J.: Acute Intussusception in Infants and Children, Ann. Surg. **124**: 262, 1946.
8. Joyce, T. M.: Tumors of the Small Intestine, Ann. Surg. **100**: 949, 1934.
9. Kempton, A. R., and Crane, A. R.: Heterotopic Gastric Mucosa, New England J. Med. **218**: 627, 1938.
10. Kohle, H. R.: Analysis of 151 Cases of Intussusception, Am. J. Surg. **52**: 215, 1941.
11. Merchant, F. T.: Intussusception Due to Hemangioma of the Jejunum, Arch. Surg. **39**: 1031, 1939.
12. Raiford, T. S.: Tumors of the Small Intestine, Arch. Surg. **25**: 122, 1934.
13. Reisinger, M.: Acute and Subacute Intussusception on the Basis of Intestinal Polypi, Deutsche Ztschr. f. chir. **227**: 255, 1930.

Editorial

The Antibiotics and Liver Injury

THE report of Markowitz, Rappaport, and Scott in 1949 that penicillin prevents death following ligation of the dog's hepatic artery is of vital concern to surgeons because it offers a new means of combating liver injury. Without the use of antibiotics the mortality rate following ligation is about 80 to 90 per cent.

Markowitz's experiments have been confirmed by later investigators. In our laboratory Scott and Mackie found that aureomycin is equally as effective as penicillin and that streptomycin has little or no protective action. The cause of death following ligation of the dog's hepatic artery is thought to be related to the growth of an anaerobic bacillus normally present in the dog's liver similar to the Welch bacillus. This bacillus has been shown by Nichols in our laboratory to be sensitive to penicillin and aureomycin but not to streptomycin, additional evidence that death is related to bacterial growth, since the first two antibiotics are effective in preventing death while the last is ineffective.

The mechanism by which ligation of the artery causes death can be explained by the oxygen supply of the liver. Although the hepatic artery is thought to carry only about a fifth of the total blood supply to the liver the percentage of total oxygen it supplies is much greater. In preliminary studies attempting to measure oxygen tension in the dog's liver by a platinum tipped electrode we found that the oxygen tension of the dog's liver is reduced to approximately the same extent by occlusion of the hepatic artery as by occlusion of the portal vein. It appears that the ligation of the artery produces a degree of liver hypoxia sufficient to allow growth of the anaerobic organisms and death either from bacterial toxins or toxins liberated from the breakdown of liver tissue. Antibiotics suppress the bacteria growth sufficiently to prevent death even though some liver necrosis may have been produced.

Do these studies have application to man? It is known that the dog's liver normally harbors anaerobic organisms, but the few bacteriological studies of the human liver, although they have not been uniform, have in general indicated that it is sterile under normal conditions. Nevertheless, before the use of antibiotics, ligation of the hepatic artery in man was fatal in most instances reported in the literature. The more distal the ligation the greater the mortality, a finding to be expected because of the decrease in collateral circulation as the artery approaches the liver. Many of the so-called "liver deaths" following cholecystectomy were probably due to inadvertent ligation of the main or right hepatic artery. Since the use of antibiotics several ligations have been reported without fatal results. Rienhoff has successfully ligated the hepatic artery in the treatment of patients with portal hypertension, using antibiotic protection.

Yet the use of the antibiotics in the treatment of liver injury in man would seem to have wider application than in the rare instances of inadvertent or deliberate ligation of the hepatic artery, or in their well-accepted role in the treatment of cholangiohepatitis from ductal obstruction. Bacteria from the blood stream are known to be filtered by Kupffer's cells of the liver. In portal bacteremia from intraperitoneal infection enormous numbers of organisms may be carried to the liver. If liver damage is already present, or if liver hypoxia has been produced by shock or local interference with blood supply, these organisms may multiply and produce a fatal liver gangrene. The value of antibiotics in the treatment of peritonitis and strangulation intestinal obstruction may be due not only to prevention of the growth of the bacteria locally but also to the prevention of their growth in the liver. In this connection the work of Opie, in 1910, is pertinent. Opie found that a combination of chloroform given by mouth and streptococci or other bacteria given intravenously resulted in death from liver injury even though neither agent given alone was sufficient to cause death or even severe injury to the liver. It seems possible that antibiotics may be effective in treating patients with liver injury produced by a variety of harmful agents during times when bacteremia is present and when the bacteria might otherwise cause a symbiotic aggravation of the injury.

—*William T. Fitts, Jr.*

ANNOUNCEMENT

On Feb. 14, 1952, the Buffalo Surgical Society presented the Roswell Park Memorial Medal for "outstanding surgical achievement" to Dr. Edward D. Churchill, of Boston, Mass.

Dr. Churchill is the fifth recipient of this award. Previous recipients have been Dr. Allen O. Whipple (1948), Dr. Evarts A. Graham (1949), Dr. Dallas B. Phemister (1950), and Dr. Frederick A. Coller (1951).

At the presentation ceremonies, Dr. Churchill delivered the annual Roswell Park Lecture, entitled, "The Architectural Basis of Pulmonary Ventilation."

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

PANCREATITIS: A REVIEW

A. C. IVY, PH.D., M.D., CHICAGO, ILL., AND G. E. GIBBS, PH.D., M.D.,*
BALTIMORE, MD.

(From the Department of Clinical Science, University of Illinois College of Medicine, Chicago, Ill.)

DEFINITION

ACUTE pancreatitis is a relatively common disease varying in intensity from a mild edema without symptoms to a generalized fulminating necrosis with severe pain, shock, and death. Chronic pancreatitis is also a relatively common disease varying in intensity from a mild localized fibrosis and/or calcification without symptoms to a generalized fibrosis with the signs and symptoms of a deficiency of pancreatic digestion and sometimes insulin production. Both acute and chronic pancreatitis, though due to numerous different causes, are frequently associated with biliary-tract disease, and the milder types are frequently unrecognized.

The acute and chronic types of pancreatitis have been variously classified. For the purpose of this presentation, the following descriptive classification will suffice:

1. Acute edematous or interstitial pancreatitis, with or without fat necrosis. (This should not be considered a lethal disease per se.)
2. Acute necrotizing, nonhemorrhagic pancreatitis, with or without fat necrosis.
3. Acute necrotizing hemorrhagic pancreatitis, with or without fat necrosis.
4. Acute suppurative pancreatitis, with or without fat necrosis.
5. Chronic relapsing pancreatitis, which probably represents repeated sublethal attacks of the acute forms of the disease, and which finally produces the sixth type:
6. Chronic pancreatitis, fibrous, calculous, or calcified in type, or with two or more of these characteristics in combination. (Senile atrophy is associated with aging or arteriosclerosis of the blood vessels.)
7. Fibrocystic pancreatitis, which is a special form of chronic pancreatitis.

Pancreatitis, in some instances, is undoubtedly progressive in nature. It may progress from mildly acute to catastrophically acute pancreatitis, or from sublethally acute to chronic pancreatitis. For example, in a series of 177 cases of acute pancreatitis, 99 or 56 per cent gave a history of previous attack.[1-4]

Presented at a Joint Session of the Sections on Pathology and Physiology and Gastroenterology, Ninety-ninth Session of American Medical Association, San Francisco, Calif., June 30, 1950.

Received for publication, June 26, 1951.

*Now a member of the Department of Pediatrics, University of Maryland.

In another series, 43 per cent quite certainly, and 61 per cent quite probably, of 307 cases of acute pancreatitis gave a history of a previous attack[5] (Table I). Furthermore, 60 per cent of 39 cases of calcification of the pancreas were associated with a history of relapsing pancreatitis, and calcification was known to have developed in 20 per cent of the cases within one year after the acute attack.[6]

TABLE I. INCIDENCE OF HISTORY OF PREVIOUS ATTACKS OF PANCREATITIS

AUTHOR	NUMBER OF CASES OF ACUTE PANCREATITIS	HISTORY OF PREVIOUS ATTACK	
		NUMBER	PER CENT
Love[1]	51	31	61
Fallis and Plain[2]	26	14	54
Lewison[3]	35	25	71
Probstein et al.[4]	65	29	45
Total	177	99	56
Paxton and Payne[5]	307	132*	43
	307	187†	61

*In 132 of the cases the diagnosis was quite certain.
†In 187 of the cases (61 per cent) the diagnosis was probably correct.

It is clear that the chief pathologic features of acute pancreatitis are either edema, necrosis, hemorrhage, or suppuration, and the chief pathologic feature of chronic pancreatitis is either fibrosis, calcification, or, in infants and children, the formation of small multiple cysts.

INCIDENCE

Our knowledge of the incidence of acute and chronic pancreatitis is quite meager. However, it is now commonly believed that the incidence of acute edematous pancreatitis, especially the subclinical variety, is greater than was formerly believed. For example, in 1939, the incidence of acute pancreatitis was given as one case in 10,000 admissions to a hospital in Detroit and, in 1949, as 1 case in 600 admissions to a hospital in St. Louis.[2, 4] The more frequently a determination of the serum amylase or lipase is made in patients with upper abdominal pain, the more frequently the acute disease will be recognized. The incidence of acute necrotizing pancreatitis in an autopsy series of 41,333 cases was 158 or 0.38 per cent.[7]

The incidence of chronic pancreatitis in a large autopsy population is uncertain because a large series of autopsies in which it is certain that the pancreas was examined routinely and carefully was not found by us. However, considerable data are available showing the very frequent association of acute pancreatitis with biliary-tract disease. A normal gall bladder was present in 30 per cent of 125 cases of acute pancreatitis[2, 3, 7] (Table II). Gallstones coexisted in 55 per cent of 667 cases of acute pancreatitis[2, 3, 7-9] (Table III). This correlation is greater than with the disease of any other organ. Gallstones were found 6 times more frequently in men and women dying with acute pancreatitis than in the general necropsy population.[11] However, acute cholecystitis was found in only 18 per cent of 238 cases of pancreatitis[2-4, 7, 10]; and acute pancreatitis was found in only 18 per cent of 163 cases of acute cholecystitis[4, 10] (Tables IV and V). The occurrence of the same percentage suggests a common

etiology, as for example, the anatomical relations or lymphatics are such in 18 per cent of persons who develop one of these diseases that the inflammation may extend in either direction.

TABLE II. INCIDENCE OF NORMAL GALL BLADDER IN PATIENTS WITH ACUTE PANCREATITIS

AUTHOR	NUMBER OF CASES OF PANCREATITIS	NORMAL GALL BLADDER	
		NUMBER	PER CENT
Fallis and Plain[2]	26	7	27
McWhorter[7]	64	25	39
Lewison[3]	35	7	20
Total	125	39	31

TABLE III. INCIDENCE OF CHOLELITHIASIS IN ACUTE PANCREATITIS

AUTHOR	NUMBER OF CASES OF ACUTE PANCREATITIS	CASES OF CHOLELITHIASIS	
		NUMBER	PER CENT
Guleke[8]	437	256	59
Egdahl[9]	105	44	42
Fallis and Plain[2]	26	15	58
McWhorter[7]	64	25	39
Lewison[3]	35	28	80
Total	667	368	55

TABLE IV. INCIDENCE OF ACUTE CHOLECYSTITIS IN ACUTE PANCREATITIS

AUTHOR	NUMBER CASES OF ACUTE PANCREATITIS	CASES OF ACUTE CHOLECYSTITIS	
		NUMBER	PER CENT
McWhorter[7]	64	14	22
Fallis and Plain[2]	26	4	15
McCorkle and Goldman[10]	43	9	21
Probstein et al.[4]	70	15	21
Lewison[3]	35	1	3
Total	238	43	18

TABLE V. INCIDENCE OF ACUTE PANCREATITIS IN ACUTE CHOLECYSTITIS

AUTHOR	NUMBER CASES OF ACUTE CHOLECYSTITIS	CASES OF ACUTE PANCREATITIS	
		NUMBER	PER CENT
Probstein et al.[4]	121	16	13
McCorkle and Goldman[10]	42	14	33
Total	163	30	18

ETIOLOGY

Analysis of the Possible Etiological Factors of Acute Pancreatitis

The factors of possible etiological significance in acute pancreatitis may be outlined as follows:

I. Infectious

A. Invasion from the blood stream, as in mumps, and in multiple abscesses of the pancreas in bacteremia and infected emboli

B. Lymphatic spread from the infected gall bladder

C. Lymphatic spread from the infected adjacent common bile duct and ampulla of Vater

D. Direct tissue spread of infection from a duodenal ulcer, duodenitis, or the common bile duct and ampulla of Vater

E. Activation of the bacteria normally present in the gland

II. Noninfectious

A. Obstruction of the pancreatic duct by:

1. Stone low in the ampulla of Vater
2. Spasm of the sphincter of the ampulla of Vater or the papilla of Vater
3. Spasm of the sphincter of the pancreatic duct
4. Edema of the papilla of Vater
5. Edema of the papilla of the pancreatic duct
6. Metaplastic plaques of the epithelium of the pancreatic ducts
7. Ascaris
8. Tumors
9. Pancreatic calculi

It should be emphasized that obstruction may occur with or without histologically detectable rupture of the ducts.

B. Chemical irritation due to:

1. Reflux of normal or abnormal bile into the pancreatic duct
2. Reflux of duodenal contents into the pancreatic duct
3. Bacterial products in the bile, or duodenal content which regurgitates into the pancreatic duct

C. Self-digestion or autolysis due to:

1. Passage of steapsin and/or trypsinogen or trypsin into the interstitial spaces
   a. By seepage through ducts and between the acinar cells secondary to increased pressure in the ducts up to the secretory pressure of pancreatic juice (30 cm. H_2O, or 22 mm. Hg) or
   b. By rupture of the ducts as may occur in vomiting, coughing, or straining in the presence of obstruction of the ducts, rupture being known to occur at 80 cm. H_2O pressure

D. Vascular disturbances

1. Venous stasis secondary to:
   a. Edema, and/or
   b. Increased pressure in the ducts (The capillary pressure is approximately 30 cm. H_2O which is the secretory pressure of pancreatic juice; a pressure of 20 to 25 cm. H_2O should cause venous stasis.)
2. Vascular spasm
3. Embolism and infarction
4. Thrombosis and venous or arterial infarction
5. Vascular necrosis due to trypsin in the interstitial spaces
6. Rupture of an arteriosclerotic vessel, called "pancreatic apoplexy."

E. Combination of several factors, such as obstruction plus passage of enzymes into interstitial tissue plus venous or arterial obstruction

F. Miscellaneous

1. Trauma
2. Alcoholism
3. Allergy
4. Diabetic Acidosis
5. Electric shock
6. Excessive action of the vagi, causing a spasm of the sphincter of the pancreatic duct, the formation of an enzyme-rich secretion, and vascular congestion
7. Zinc ingestion (chronic pancreatitis)[116]
8. Fatty meal during the early remission from attack of acute pancreatitis
9. Degenerative changes due to tumors, and vascular degenerative changes (chronic pancreatitis chiefly)

Evidence on the Etiology of Acute Pancreatitis

I. *Is Infection the Cause of Acute Pancreatitis?*—Thirty years ago infection was quite widely accepted as the cause of acute pancreatitis.[12, 13] It was known that multiple abscesses of the pancreas or a suppurative pancreatitis sometimes occurred in diseases which were associated with a bacteremia such as typhoid and scarlet fever or the production of infected emboli. But since bacteremia was uncommon in acute pancreatitis, and since biliary-tract disease was found to be associated frequently with pancreatitis, the view that pancreatitis is due to a lymphatic spread from the gall bladder was proposed. When it was found that the gall bladder was not always diseased, the idea that a bacterial inflammation could spread from the common bile duct, a duodenal ulcer, or duodenitis was suggested. This, of course, could and does occur and is a cause of a local pancreatitis of the adjacent pancreas. When it was found that bile could undergo reflux into the pancreatic duct, it was suggested that the effect of the infection was added to that of the reflux.[14] When it was discovered that bacteria are found in many normal tissues, including the pancreas, it was hypothesized that bacteria, when found, represented the activation of those normally present,[15] or those which invaded secondarily and enhanced the severity and lethality of the disease. (For a review of this literature see references 3 and 5.)

The evidence on the relation of infection to pancreatitis will be briefly summarized.

A. *The experimental evidence:* (1) Bacteria have been seen in the pancreatic duct of a dog with a pancreatic fistula without the development of acute pancreatitis or hemorrhagic necrosis of the pancreas.[16] However, infection may apparently cause acute pancreatitis with glycosuria occasionally in dogs with pancreatic fistulas. The pathologic picture is that of an acute edematous pancreatitis.[17] Since edematous pancreatitis can occur in the presence of *Escherichia*

coli and streptococci in the pancreatic ducts and in the absence of a *known* obstruction, it is reasonable to suspect the bacteria as the cause. Such a conclusion is equivocal because it is possible that an obstruction of the pancreatic duct had occurred and had corrected itself unknown to the investigator. (2) That bacteria in the ducts may contribute in part to the development of pancreatitis is indicated by the following observation. Nordman,[83] who operated on dogs so as to cause bile to reflux into the pancreatic duct, found that pancreatitis developed only when the bile was deliberately infected by him. (3) However, the production of an acute infection of the gall bladder or biliary-tract injection of bacteria into the pancreatic parenchyma of experimental animals does not cause acute pancreatitis.[13, 18] (4) Anatomically, Kodama[19] reports that there are no lymphatic connections between the gall bladder and pancreas through which an infection might spread, though such connections do exist between the intramural portion of the common duct and the pancreas. In our opinion the claim that there are no lymphatic connections between the gall bladder and pancreas would bear further study in man, since such connections may be present in some persons and not in others. This is based on the observation, in a patient, of edematous pancreatitis in association with acute cholecystitis in the presence of the probable separation of the orifices of the pancreatic and bile ducts.[17] (5) The injection of bacterial suspensions into the pancreatic duct will cause pancreatitis,[14] but the sterilized suspension will do the same.[16]

COMMENT.—The experimental evidence provides meager support for infections as the cause of pancreatitis. It records only that the presence of bacteria or their products in the pancreatic duct, with or without bile, may occasionally appear to contribute to the cause of pancreatitis. One cannot be certain that in such instances temporary obstruction of the pancreatic duct did not contribute to, or actually cause, the pancreatitis. However, bacteria as a contributory factor cannot be ruled out in some cases of experimental pancreatitis.

B. *The clinical evidence:* (1) Several careful investigators have obtained sterile cultures from the pancreas in as many as 50 per cent of their cases of pancreatitis.[16] (2) The gall bladder has been found to be normal in 30 per cent of 125 cases of acute pancreatitis[2, 3, 7] (Table II). (3) Only 18 per cent of 238 cases of acute pancreatitis had an associated acute cholecystitis[2-4, 7, 10] (Table IV). (4) Only 18 per cent of 163 cases of acute cholecystitis had acute pancreatitis[4, 10] (Table V). Spread of infection or inflammation would be suspected when reflux is impossible. In some such cases the gall bladder, the structures of the hepatoduodenal ligament, and the pancreas are edematous without involvement of other upper abdominal structures. In these cases it would be important for the pathologist to ascertain if reflux of bile was impossible. If so, spread of infection or inflammation through the tissue spaces or lymphatics should be suspected. In the case of anatomical separation of the ducts, with the concomitant occurrence of acute cholecystitis and pancreatitis, either spread of infection or inflammation is involved, or a duodenitis with edema of the pancreatic papilla, or spasm of the sphincter of the pancreatic duct would have to be the cause of the obstruction of the pancreatic duct and the pancreatitis. (5) Nevertheless, the statistics show that acute pancreatitis is more commonly

associated with chronic cholecystitis and cholelithiasis than with acute cholecystitis. Cholelithiasis was present in 55 per cent (40 to 80 per cent) of 667 cases of acute pancreatitis[2, 3, 7-9] (Table III).

Summary: Infection is occasionally the cause of pancreatitis by invasion through the blood stream and by extension from the gall bladder via the structures of the hepatoduodenal ligament. Infection or bacterially contaminated inflammation may extend from a duodenal ulcer or the intrapancreatic and intramural portion of the bile duct to the pancreas causing a more or less localized pancreatitis. Bacterial infection of the pancreatic ducts in the absence of obstruction cannot be claimed to be a sole cause of pancreatitis.

The association between biliary-tract pathology and pancreatitis means that when there is a tendency to spastic or edematous closure of the outflow of bile, the same tends to exist for the outflow of pancreatic juice. It is well known that obstruction to bile outflow predisposes to, and sometimes causes, pathology of the biliary tract, and obstruction to pancreatic outflow predisposes to and sometimes causes pathology of the pancreas. The mechanisms for the outflow of bile and of pancreatic juice are so closely related anatomically and physiologically that one can hardly be involved without the other. In fact, it is surprising to a physiologist that the correlation between pathologic changes in the biliary tract and in the pancreas is not higher than one finds reported in the available literature.

Acute Pancreatitis in Mumps.—Acute pancreatitis in mumps, though an infectious process, has a bearing on the question of the noninfectious etiology of acute pancreatitis.

In mumps, the parotid gland, though markedly edematous, does not manifest either fat or vascular necrosis. The pancreatitis which occurs definitely in 2.4 per cent of patients with mumps[20] is usually only edematous in type. Occasionally, however, the edematous pancreatitis becomes complicated with fat and vascular necrosis. This occurs in the absence of any reported obstruction of the outlet of the pancreatic duct or reflux of bile into the pancreatic duct. In such instances it would appear that the edema becomes so marked that the blood flow of the organ is impaired and self-digestion with or without vascular necrosis and hemorrhage results.

It should be pointed out that the diagnostic value of the serum amylase in mumps is handicapped by the fact that the elevated amylase may come from the parotid gland. For example, Applebaum[21] found the serum amylase elevated in 48 of 50 cases of parotitis. This may or may not indicate the involvement of the pancreas. Clinically, Poppel and Bacon[22] observed the signs and symptoms of pancreatitis in only 17 of 95 cases of parotid mumps with positive roentgenographic evidence of pancreatitis in only 7 of the 14 so examined. Bass and Tudor,[23] who observed elevated serum amylase values in 12 of 15 cases of mumps, found markedly elevated amylase values in one patient with definite pancreatitis. Since we now know[41] that a subclinical pancreatitis may occur in the presence of only slightly elevated serum amylase, it may be that most patients with mumps have an involvement of the pancreas. However, Caudel and Wheelock[24] found the serum lipase elevated in only 12 per cent, whereas the serum amylase

was elevated in 84 per cent, of 224 patients with mumps. This would indicate that the pancreas is only occasionally involved in mumps and that the high incidence of elevated serum amylase is due only to the involvement of the parotid gland.

II. *Is Acute Pancreatitis Due to a Noninfectious Cause?*

A. *Obstruction of the pancreatic duct:* Obstruction of the papillary orifice of the ampulla of Vater could occur as a result of the presence of a small stone located at, or edema of, the papillary orifice of the ampulla, or as a result of a spasm of the sphincter of the ampulla or papilla in some persons.

ANATOMY.—A diagram of the anatomy of the sphincter is shown in Fig. 1; the more detailed anatomy has been carefully studied and described by Kreilkamp and Boyden.[25]

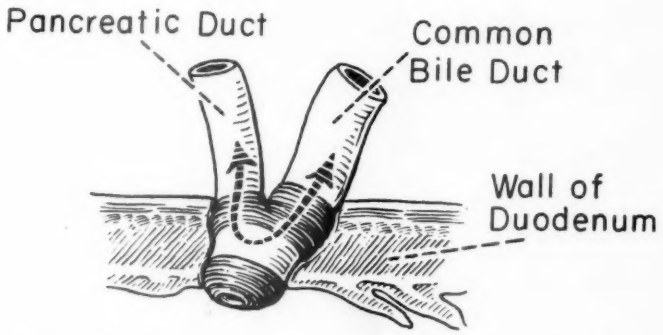


Fig. 1.—The intramural portion of the common bile duct in which the common bile duct joins with the chief pancreatic duct or the duct of Wirsung to form a common ampulla which opens through the papilla. The circular lines represent the sphincter of the common bile duct, of the duct of Wirsung, and of the lower portion of the ampulla of the papilla.

Anatomically, the presence of a small stone at, or edema of, the papillary orifice, or spasm of the sphincter of the lower ampulla could cause reflux of bile into the pancreatic duct and cause temporary obstruction to pancreatic outflow in from 30 per cent to 70 per cent of persons[26-37] (Table VI). The figure of 30 per cent is obtained from dissections and an estimate of the possibility of reflux is made on the basis of the pancreatic duct joining the bile duct 2 mm. or more distal to the papillary orifice. The figure of 70 per cent is obtained from experiments in which the papilla is occluded and the bile duct injected with radiopaque media or a colored fluid. During cholangiography the pancreatic duct may be visualized in approximately 36 per cent of patients (Table VII). Repeated attempts to visualize the pancreatic duct would undoubtedly increase the percentage so that it would approach the maximum possible percentage of 70 per cent. The exact percentage possible will always remain moot, but it will certainly be higher than 30 per cent and less than 70 per cent (Tables VI and VII).

A fact that has not been mentioned in the literature but which should be emphasized is as follows: When the pancreatic duct opens very close to, or at, the orifice of the papilla of Vater or when the pancreatic duct open separately

TABLE VI. SHOWING THE ANATOMIC RELATION BETWEEN THE PANCREATIC AND COMMON BILE DUCT IN MAN

AUTHOR	TOTAL NUMBER CASES	DUCTS OPEN SEPARATELY		COMMON AMPULLA		PANCREATIC DUCT OPEN 2 TO 3 MM. OR MORE ABOVE PAPILLA PERMITTING REFLUX	
		NUMBER CASES	PER CENT	NUMBER CASES	PER CENT	NUMBER CASES	PER CENT
Anatomical Dissection							
Opie[26]	100	11	11	89	89	28	28*
Mann and Giordano[27]	192	62	32	130	68	42	20
Baldwin[28]	90	20	22	70	78	58	64
Belou[29]	50	27	54	23	46	8	16
Rienhoff and Pickrell[30]	246	73	29	173	71	81	32
Total	678	193	29	485	71	217	32
Occlusion of Papillary Orifice and Injection of Bile Duct							
Millbourn[31]	200	29	15	—	—	171	85
Hjorth[32]	100	14	14	—	—	86	86
Cameron and Noble[33]	100	26	26	—	—	66	66
Howard and Jones[34]	150	41	27	—	—	81	54
Total	550	110	20	—	—	404	73
Dissection Data Incomplete for Determining Potential Reflux							
Mehnen[35]	449	175	39	274	61	—	—
Schirmer[36]	47	22	47	25	53	—	—
Ruge[37]	43	11	25	32	75	—	—
Grand Totals	1767	511	29	816	46	—	—

*In 21 of 75 cases, the pancreatic duct joined the common bile duct 2.5 mm. proximal to the papilla.

TABLE VII. INCIDENCE OF VISUALIZATION OF PANCREATIC DUCT DURING CHOLANGIOGRAPHY

AUTHOR	NUMBER PATIENTS	NUMBER VISUALIZED	PER CENT VISUALIZED
Hunt, Hicken, Best[38]	56	5	9
Robins and Hermanson[39]	25	4	16
Colp and Doubilet[40]	35	7	20
Leven[41]	91	24	26
Howell and Bergh[42]	64	27	42
Hjorth[32]	430	202	47
Liedberg[43]	53	22	41
Millbourn[31]	181	72	40
Rudstrom[44]	329	110	33
Hulten[45]	110	26	24
Stenstrom[46]	57	4	7
Total	1431	503	35

from the common bile duct, a spasm of the sphincter of the pancreatic duct, or edema of the papilla, or a pancreatic stone could mechanically obstruct the outflow of pancreatic juice even though a reflux of bile cannot occur.

Rich and Duff,[16] who emphasized the importance of obstruction of the pancreatic ducts as a cause of pancreatitis, found metaplastic plaques in the ducts of 18 per cent of 150 persons above the age of 24 years. They found the condition in 13, or approximately one-half of 24 cases of acute pancreatitis they studied. The ducts were dilated proximal to the metaplastic plaques and the pancreatitis was ascribed to the rupture of these cyst-like dilatations. Yotuy-

anagi[47] found metaplasis of the ducts in 64 per cent of human specimens and suggested that it might be due to a vitamin A deficiency and irritation of the ductal epithelium by local stasis. Clark[48] found metaplasia of the ducts in only 11 per cent of 36 cases of pancreatitis which was the same incidence he found in his control cases. Metaplasia, due to narrowing of the lumen of the duct quite obviously could cause or predispose to obstruction, especially when a viscid secretion is formed.

Ascaris in the pancreatic duct has been found in 50 autopsies of patients who died of acute pancreatitis.[49] The worm certainly caused obstruction and in addition may have irritated the duct.

Since the obstruction of the papillary orifice of the common duct by a small stone is found in only 5 per cent of cases of acute pancreatitis (Table VIII),[8, 9, 49, 50] and since obstruction of the pancreatic duct by Ascaris,[49, 52] tumors[53] and pancreatic calculi[54] is relatively rare; edema[55, 56] and spasm[57, 58] would be responsible for most of the cases of obstruction to pancreatic outflow.

TABLE VIII. ACUTE PANCREATITIS IN PATIENTS WITH A SMALL STONE AT THE PAPILLA OF VATER

AUTHOR	NUMBER OF CASES OF PANCREATITIS	CASES WITH STONE AT PAPILLA	
		NUMBER	PER CENT
Guleke[8]	437	6	1.4
Schmieden and Sebening[49]	1278	57	4.5
Smyth*[50]	245	32	13.0
Egdahl[9]	44	3	6.8
Total	2004	98	5

*Does not cite authors.

Inflammation of the epithelium of the pancreatic ducts could cause obstruction. In this connection it should be pointed out that duodenitis is a factor which could cause edema of the papilla of Vater or of the pancreatic duct when the latter opens separately from the common bile duct. No other cause of edema of the papilla is readily apparent.

The factors which cause contraction of the sphincter of Oddi in man and predispose to reflux into the pancreatic duct may be summarized as follows[58, 63]: (a) Acute, painful distention of the common bile duct causes a contraction of the sphincter which may last for from 5 to 20 minutes after the distention stimulus has been withdrawn, and the contraction of the sphincter per se may be so vigorous as to cause pain.[59, 60] (b) Emotional disturbances may cause contraction of the sphincter.[61] (c) The introduction of 0.1 N HCl into the duodenum, causes the sphincter of the lower ampulla to contract.[61, 62] Duodenitis may increase the irritability of the sphincter. (d) Morphine (1/6 gr.) causes the sphincter to contract and the contraction may continue for 20 to 40 minutes, and be vigorous enough to cause pain for a few minutes.[59, 62] (e) Parasympathomimetic agents, such as pilocarpine, Mecholyl Chloride, and Urecholine Chloride frequently cause the sphincter to contract.[63] (f) Irritation of the colon, will cause a reflex contraction of the sphincter in the dog. Although this has not been demonstrated in man, we suspect that it is true.[63]

The same factors may also cause the sphincter of the pancreatic duct to contract, although we have little evidence on the subject.

Is obstruction of the pancreatic duct alone adequate to cause evidences of pancreatitis?[64]

Pressure Relationships.—The pressure relationships which are significant in a consideration of the relation of obstruction of the pancreatic duct to pancreatitis may be summarized as follows: (a) The secretory pressure of bile and pancreatic juice (dog) is approximately 30 cm. of H_2O. There is no good evidence showing that the secretory pressure of bile and pancreatic juice are significantly different. (b) The capacity of the gall bladder to contract and exert force on its content is approximately 25 cm. of H_2O (dog). (c) The capacity of the sphincter of Oddi or the intramural portion of the common bile duct to offer resistance to the flow of fluid from the duct into the duodenum is 75 to 80 cm. of H_2O (dog and man).[63] The resistance which the sphincter of the lower ampulla may offer is conjectural, but it is known that reflux from the bile duct into the pancreatic duct will occur at a pressure of 20 to 42 cm. H_2O.[42] (d) The pressure in the common bile duct may rise to 100 cm. of H_2O during vomiting, coughing, or straining.[27] (e) The pressure required to cause rupture of the pancreatic ducts requires further investigation. Mann and Giordano[27] have reported that 80 to 600 cm. H_2O pressure was required to rupture the ducts of the goat. Rich and Duff[16] have reported that a volume of 3 to 10 c.c. of India ink injected into the chief duct of a dog will cause rupture. Popper,[65] however, has reported that rupture does not occur with 3 c.c. of India ink.

Table IX. Data Available on the Percentage of Persons in Whom the Duct of Santorini (Accessory Duct) Could Function for the Pancreas When the Terminal Portion of the Duct of Wirsung (Chief Duct) Was Occluded*

Author	Number cases	Cases where accessory duct could function	
		Number cases	Per cent
Opie[26]	100	48	48
Keyl[66]	107	56	52
Millbourn[31]	182	60	33
Hjorth[32]	100	29	29
Howard and Jones[34]	160	54†	36
Rienhoff and Pickrell[30]	100	62	62
Baldwin[28]	50	39	78
Total	789	348	44

*The accessory duct is quite patent in from 10 to 20 per cent of cases. The accessory duct is obliterated at its duodenal end in from 10 to 20 per cent of cases. The chief and accessory duct do not connect in from 1 to 12 per cent of cases.

†Accessory duct was patent at both ends in 44 of 81 cases in which reflux occurred and in only 10 of 79 in which reflux did not occur.

It might be objected that any pressure exerted through the duct of Wirsung in man would be equalized through its connections with the accessory duct of Santorini, since the accessory duct connects with the intestine and with the chief duct of Wirsung. In the dog the communication between the two ducts is so frequently functional that the smaller duct (duct of Wirsung in the dog) is always tied in physiologic studies. In man it has been found that the two ducts communicate so that the accessory duct could function if the chief duct were occluded in 40 per cent of persons (Table IX). However, the duct which

communicates between the chief and accessory duct is sufficiently wide to permit a free communication in only about 15 per cent of persons.[26, 28, 30-33, 66] So, it is not surprising, as will be indicated later[42] that a temporary reflux of fluid from the common bile duct into the chief pancreatic duct at physiologic pressures will cause a rise in serum amylase in most persons. While the patent collateral accessory duct system will not necessarily prevent a biliary reflux from causing a rise in serum amylase[42]; the degree of rise will depend on the extent of the functional competence of the accessory duct.

Nabatoff[67] thought that if obstruction of the pancreatic duct was involved in the genesis of pancreatitis, the pancreatic duct at autopsy should be found to be dilated in such cases. His study revealed no correlation. But one should expect dilation of the duct to occur only in the relapsing type of pancreatitis. Furthermore, Rich and Duff[16] found some dilation proximal to metaplastic plaques in the ducts.

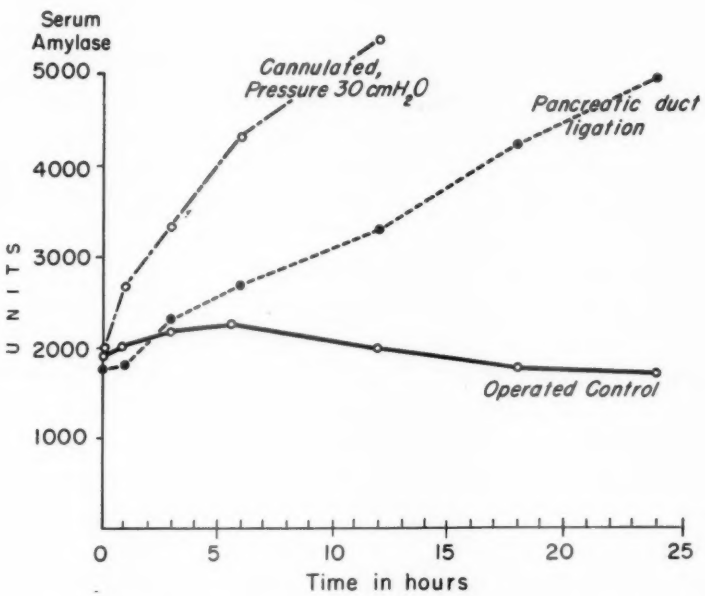


Fig. 2.—Graph showing that when the unstimulated pancreatic outflow is obstructed the serum amylase rises in 2 to 5 hours and when the duct is obstructed at the secretory pressure of pancreatic juice and maintained there the serum amylase rises in 30 to 60 minutes, or very rapidly.

Rise in Serum Amylase.—We have found that when the pancreatic ducts of a dog which has fasted 12 hours are tied, the serum amylase is definitely increased after from 2 to 5 hours. When the ducts are tied and distended with normal saline solution at a sustained pressure of 30 cm. H_2O, the serum amylase is increased within one hour. This was done to simulate a rapidly secreting gland (Fig. 2). When the chief pancreatic duct of a dog is injected with from 0.1 to 3.0 c.c. of bile or olive oil, and the ducts tied, edema of the pancreas will occur within one hour, and the serum amylase will be definitely elevated in from 2 to 5 hours.[65, 69] When bile is injected into the pancreatic duct of dogs, the serum amylase is increased within one hour.[70]

The lowest duct pressure at which amylase will regurgitate into the blood has not been determined in animals, but in man it is known to be less than 30 cm. of H_2O. Howell and Bergh[42] have made the very important observation that when during the course of cholangiography, the radiopaque material (35 per cent Diodrast or Thorotrast) or bile passes into the pancreatic duct under a pressure of from 20 to 42 cm. of H_2O, a rise of serum amylase occurs within 30 minutes and it remains elevated for from a few hours up to 48 hours. The pressure in the bile duct was greater than 30 cm. of H_2O in only 4 of 25 patients in whom a reflux and rise in serum amylase occurred; a rise did not occur unless a reflux occurred. Thus, a rise of serum amylase occurred like that observed in subclinical or mild acute edematous pancreatitis. A similar observation was made by Liedberg[43] who found diastasuria in patients in whom biliary-pancreatic reflux occurred during cholangiography.

Another observation showing the sensitivity of the pancreas to obstruction of its ducts is the elevation of serum amylase on the intravenous injection of secretin after the administration of morphine or Mecholyl, or Urecholine given with the idea of contracting the sphincter and obstructing the outflow of pancreatic juice.[69, 71, 72] The interpretation of the rise in serum amylase after the injection of secretin alone in patients with suspected acute pancreatitis is not so clear,[73] unless the edema of the pancreas causes some obstruction of the ducts without significantly impairing the capacity of the pancreas to secrete. It would be of interest to use this test in patients with parotid mumps along with the lipase test.

It is pertinent to point out that the urine amylase has been found to be elevated in 12 per cent of cases of cholecystitis, 17 per cent of cases of uncomplicated cholelithiasis, 41 per cent of cases with carcinoma of the head of the pancreas and penetrating duodenal ulcer, and 61 per cent of cases with a common duct stone.[10, 74, 75] Since it is not reasonable to suspect the presence of a generalized pancreatitis in all these patients, it is evident that a localized pancreatitis or obstruction of part of the duct system may cause an elevation of serum amylase. Bockus[76] has observed that peritonitis may be associated with an elevated serum amylase.

It is important to realize that the serum amylase in acute pancreatitis may rise and fall within a few hours, or continue at a high level for a week, or fluctuate above and within the normal limits during a period of a week or longer. The variation in the serum amylase values has been emphasized by McCorkle and Goldman,[10] who along with others[5] have pointed out that the serum amylase may be normal or less than normal after the pancreas has been practically destroyed or the blood flow through it markedly reduced by hemorrhage or necrosis.

In the presence of complete obstruction of the ducts of the rabbit, the secretory response to secretin and pancreozymin is markedly reduced in 24 hours and is very poor after four days.[77] Thus, a rapid drop in an elevated serum amylase may mean either recovery or a marked loss of the secretory capacity of the pancreas. This also indicates that when obstruction occurs in pancreatitis, it is seldom complete, otherwise the pancreas would "burn out"

in a few days. Conversely it suggests that incomplete obstruction may be a more potent etiologic factor in the genesis of pancreatitis than complete obstruction.

An understanding of the route of passage of the pancreatic enzymes into the blood is pertinent to the interpretation of the serum levels. It has been found that, although some of the amylase enters the blood by way of the lymphatics,[78] the major portion enters the blood of the pancreatic vein.[70] Thus, if pressure due to swelling would markedly reduce the blood flow, or if the veins were thrombosed, the amount of enzyme entering the circulation would be proportionately reduced. Prior to entering the blood or lymph, the enzymes are found in the interstitial edema fluid.[65] The edema fluid in edematous pancreatitis contains all the pancreatic enzymes, though in quantities inadequate to cause macroscopic fat necrosis and vascular necrosis. When the pancreas becomes quite edematous the enzymes in the fluid seep through the capsule into the peritoneum,[65] where they are absorbed into the blood (Fig. 3).

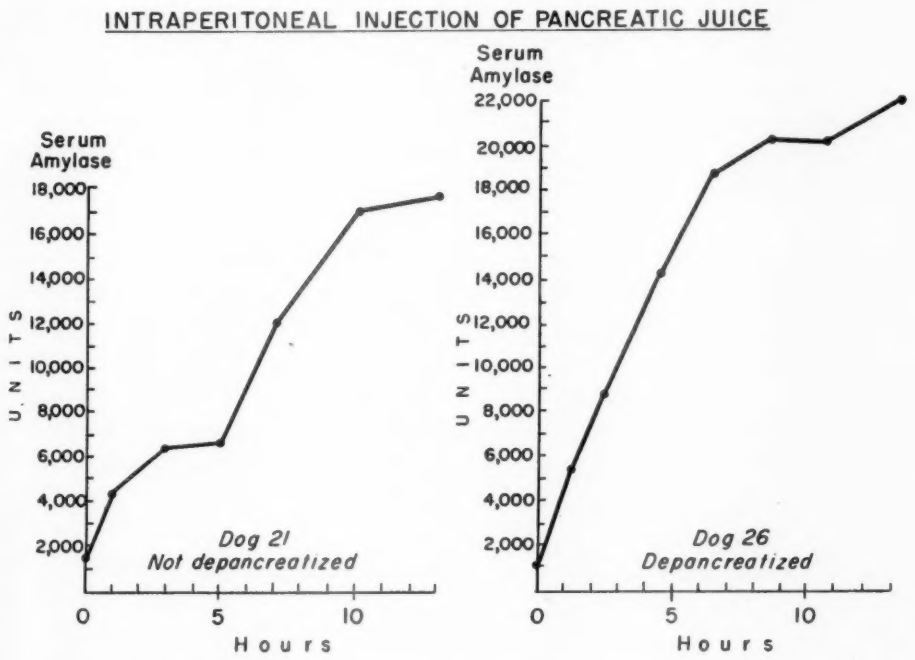


Fig. 3.—Graph showing that the presence of pancreatic juice containing amylase in the peritoneal cavity will cause a rise in serum amylase.

It has been suggested that the serum amylase in case of trauma to the pancreas may be elevated by peritoneal absorption[75] and some correlation between the serum level and that of the peritoneal exudate exists.[79, 80] The results of our experiments show clearly that amylase in the peritoneal exudate contributes to the serum level. This source is probably not as large as that which is absorbed directly into the pancreatic venous blood.[70] In the presence of such peritoneal effusion the patient probably benefits from its removal when the abdomen is opened.

SUMMARY.—The evidence shows that obstruction alone in the presence of a secreting pancreas will cause edema of the pancreas with a rise in serum amylase. Obstruction plays a very important role and may be a sine qua non in the genesis of most cases of pancreatitis.

B. *Chemical irritation:* It is commonly stated that reflux of bile into the pancreatic duct initiates pancreatitis due to its irritating properties which are proportional to the bile salt concentration of the bile used. However, in most of the experiments on which this statement is based relatively large volumes (5 to 10 c.c.) of bile have been injected, which according to some investigators causes a rupture of the ducts. Furthermore, the injection of similar volumes of trypsin solution and other substances will also cause pancreatitis.[14-16, 27, 65, 70, 81]

Because pancreatic juice has been found to undergo reflux into the gall bladder under certain conditions and to be found there in some cases of cholecystitis, it has been concluded that pancreatic juice irritates the gall bladder mucosa and causes cholecystitis. However, in the dog, if the strip of duodenum into which the chief pancreatic duct empties is carefully anastomosed to the gall bladder and the accessory pancreatic duct is tied so that all the pancreatic juice, after being activated by the intestinal secretion, flows into the gall bladder and thence into the cystic and common ducts and the duodenum, no cholecystitis occurs.[82] However, if the operation is not done carefully so that tissue trauma is avoided, gangrenous, hemorrhagic cholecystitis, will occur[82]; the same is true when the cystic duct is obstructed, or the blood supply of the gall bladder occluded.

In order to avoid abnormal pressures rupturing the pancreatic duct, Nordman[83] Mann and Giordano,[27] Bisgard and Baker,[84] Wangensteen and co-workers,[18] and Tejerina-Fotheriugham[14] operated on goats, rats, dogs, and cats so that bile could undergo a reflux into the pancreatic duct. The results reported may be summarized as follows: The passage of bile into the pancreatic duct under possible in vivo conditions of pressure did not cause pancreatitis in the relatively few experiments performed in the mature goat, rat, and dog; it did cause pancreatitis in the young goat and the cat, particularly when the cat was fed a fatty meal with the idea of causing contraction of the gall bladder.

SUMMARY.—There is no evidence showing that the presence of bile in the pancreatic ducts in the absence of rupture of the ducts or temporary obstruction of the outflow of pancreatic juice will cause a rise in serum amylase or cause pancreatitis. Even in the observations of Howell and Bergh, referred to previously, the reflux of the x-ray contrast media or bile into the pancreatic duct was associated with a temporary obstruction to the outflow of pancreatic juice.

There is good reason to believe that if some bile, along with pancreatic juice should enter the interstitial tissues, the irritating qualities of bile salts would facilitate the action of the enzymes of the pancreatic juice on the irritated tissues.

When Rich and Duff[16a] injected bile into the salivary duct (pressure of the injection was not given), tissue damage was obtained, but there was nothing analagous to fat and vascular necrosis. *It should be emphasized that typical*

fat necrosis and vascular necrosis are characteristic of pancreatic disease only, and can never come except from the pancreatic enzymes, steapsin, and trypsin, and from them only when they are outside the pancreatic ducts and intestine.

Finally, acute pancreatitis occurs in patients in whom the pancreatic duct opens separately. According to our search of the literature 9 such cases have been reported. Popper,[85] Dardinski,[86] and Rich and Duff[16] report 2 cases each, and Johnstone,[87] New,[88] and Simkims[89] one case each. Mann and Giordano[27] state that they had seen such cases but do not say how many. *This observation shows that the reflux of bile is not necessary for the genesis of pancreatitis.* In such patients, however, obstruction to pancreatic outflow can be due to other causes.

C. Self-digestion or autolysis: The digestive action of pancreatic juice when outside the ducts and intestine has been described well by Rich and Duff.[16] Their observations may be summarized as follows: (1) The subcutaneous injection of 0.3 to 0.8 c.c. of nonactivated or very dilute activated juice causes only a mild irritation. (2) The subcutaneous injection of 0.3 to 0.8 c.c. of activated dilute juice causes fat necrosis. (3) The injection of 0.3 to 0.8 c.c. of viscid juice, which is usually active as collected from the pancreatic duct, causes fat and vascular necrosis like that seen in necrotizing hemorrhagic necrosis. (4) The subcutaneous injection of a similar volume of bile causes only a local edema. (5) As pointed out previously, when trypsin solution or papain solution is injected into the pancreatic duct so as to cause a rupture of the ducts, a typical vascular necrosis occurs.

Whether the steapsin and trypsin enter the interstitial spaces by seepage or by rupture of the ducts is an academic question. *The fact is that they must get there in adequate concentration; and when they do, they cause fat and vascular necrosis.*

The activation of trypsinogen in or out of the ducts is not a difficult problem, since it has been known to gastrointestinal physiologists for 35 years that trypsinogen is easily activated. Active trypsin is frequently found in the normal pancreatic duct when the juice is viscid or stimulated by vagal action.[90, 91] The addition of calcium to the juice, the addition of bile, tissue juice, or leukocytes, as well as enterokinase change trypsinogen to trypsin (92), facts which have been frequently confirmed by one of us (A.C.I.). However, as shown by the experiments of Rich and Duff[16a] the pancreatic juice activated with enterokinase in much more necrotizing when injected subcutaneously than juice which has not been activated. So, the activation of pancreatic juice by tissue juices is not as potent as by enterokinase. Another point which has to be considered in this regard is the specific trypsin inhibitor in the pancreas, a substance which has been crystallized and probably serves as a protective factor.[16b]

When one observes the development of acute pancreatitis, three stages of severity may be seen. First, obstruction causes an interstitial edema. Second, when the edema is marked, fat necrosis occurs, due to obstruction in the presence of copious secretion, particularly at pressure points or in mildly traumatized areas. Vascular lesions are small, patchy, and not always easy to find. The third stage is dramatically characterized by the gangrenous or necrotizing,

hemorrhagic necrosis, the like of which occurs at no other place in the body. Something in addition to obstruction plus secretion is involved in the cause of this catastrophic pathology. From the experimental observation, the additional factor is either rupture of the ducts with the spillage and activation of adequate concentrations of trypsinogen, or a vascular disturbance.

D. *Vascular disturbances:* A good active blood flow is the most important factor preventing self-digestion.[93] So vascular disturbances should play an important role in determining the severity of acute pancreatitis.

Hemorrhage into the pancreas in acute pancreatitis could be due to the following disturbances: (a) vascular necrosis due to the digestion of the blood vessel wall and the release of blood, (b) venous thrombosis which would cause the picture of a "wet gangrene," (c) rupture of an arteriosclerotic artery, causing "pancreatic apoplexy," (d) purpura, or delayed coagulation of the blood, or a vasomotor dyscrasia. Arterial occlusion or generalized arteriolar spasm or thrombosis would be required to explain an ischemic necrosis of the pancreas. It is much easier to visualize how necrosis of the pancreas occurs with hemorrhage than without hemorrhage.

Venous stasis could be caused by the edema of the gland or an increase in pressure in the ducts due to obstruction. Venous stasis would predispose to thrombosis and digestion of the vein. A pressure in the ducts or within the capsule of the pancreas of 20. to 25. cm. of H_2O, somewhat less than the secretory pressure, should cause some venous stasis. Decreased blood flow would predispose to digestion.

It is not easy to explain the source of a vascular spasm leading to schemia, although we know that ischemic necrosis occurs in the gastric mucosa.[93]

EXPERIMENTAL PRODUCTION OF THE VARIOUS TYPES OF ACUTE PANCREATITIS

All the various types of acute pancreatitis which occur most commonly have been produced experimentally.

Acute Edematous or Interstitial Pancreatitis.—

Animals: Simple obstruction of the pancreatic ducts causes edematous pancreatitis which, if continued, results in atrophy of the acinar tissue with but little proliferative fibrosis in the dog and the rabbit.[77, 94] When the ducts are tied in the presence of copious secretion the edema is evident within 30 minutes and the enzymes in a low concentration are found in the interstitial fluid.[65, 68] Wangensteen and co-workers[18] report that rupture of the ductules occurs in cats along with the edema. When a pressure of 30 cm. of normal saline is maintained in the pancreatic ducts of a dog, edema develops rapidly and serum amylase rises rapidly.[94] Fat necrosis occurs at any point of pressure trauma, and focal necrosis about small ductules is evident at 12 to 24 hours. It has not been proved that the injection of a small quantity of bile (0.1 to 1 c.c.) into the obstructed ducts will speed the rate of development or increase the incidence of fat necrosis, although amounts which rupture the ducts will do so.[68, 81]

Man: As indicated before, Howell and Bergh[42] made the important discovery that in 52 patients the reflux into the pancreatic duct of Diodrast or

Thorotrast (35 per cent), mixed with some bile, caused a rise in serum amylase within 30 minutes, and it remained elevated in some patients for 48 hours. In all but 4 patients the pressure under which reflux occurred was less than 30 cm. H_2O. In two of four patients in whom the pressure was between 30 and 42 cm. of H_2O the clinical symptoms of acute pancreatitis occurred.

Comment: The evidence in animals and man shows that acute edematous pancreatitis will occur when the pancreatic ducts are obstructed in the presence of secretion. Whether fat necrosis develops depends on the rate of secretion and pressure trauma. In man, the obstruction need be only temporary (10 to 30 minutes) and may be due to biliary reflux into the pancreatic duct under a pressure of 25 to 42 cm. of H_2O pressure.

Acute Necrotizing, Hemorrhagic Pancreatitis.—Acute necrotizing, hemorrhagic pancreatitis may be produced experimentally. (a) It occurs quite uniformly in animals after the production of obstruction with rupture of the pancreatic ducts containing secretion by the injection of bile or trypsin solution. In man, distention of the obstructed pancreatic ducts containing secretion, or a mixture of secretion and bile, caused by the pressure which occurs in vomiting or coughing, (100 cm. H_2O) theoretically could rupture the ducts.[14-16, 27, 65, 70, 81] (b) The injection of mercury droplets into the pancreatic artery caused hemorrhagic necrotizing pancreatitis to occur in the dog after from 20 to 72 hours.[50] It should be self-evident that the pancreas will digest itself if it is deprived of all, or much, of its blood supply.[93] This is not true of the stomach because pepsinogen is activated by acid and acid is required for the action of pepsin. Trypsinogen becomes activated on deprivation of blood supply, and trypsin acts at a slightly acid or alkaline pH. (The pancreas of some animals has a rich collateral circulation and the tying of a few vessels has no effect.)

Acute Necrotizing, Nonhemorrhagic Pancreatitis.—Acute necrotizing, nonhemorrhagic pancreatitis may be produced experimentally as follows: (a) The pancreatic ducts of a dog are obstructed during the presence and maintenance of a rapid secretion, and then the pancreatic artery is occluded for 15 minutes. Or, obstruction plus copious secretion plus ischemia for 15 minutes gives an "ischemic necrosis" of the pancreas. Since the same procedure may also cause acute necrotizing, hemorrhagic pancreatitis,[68] further investigation of the mechanism of this type of pancreatitis is needed.

"Parasympathetic Pancreatitis."—Parasympathomimetic drugs cause the secretion of a viscid pancreatic juice rich in enzyme, a vasodilation, and probably a contraction of the sphincter of the pancreatic duct, since we know they contract the sphincter of Oddi. When given repeatedly they cause vacuolization of the acinar cells.[95]

If the pancreatic duct is tied in a dog or a cat and pilocarpine is injected, an edematous pancreatitis with or without fat necrosis and a small amount of patchy vascular necrosis frequently occurs.[96, 97] Without the obstruction of the ducts, Mecholyl given repeatedly or continuously will cause an edematous pancreatitis with a variable amount of fat and patchy vascular necrosis in the dog.[98] It is reported that the administration of pilocarpine three times daily to kittens will cause achylia pancreatica.[99]

"Alcoholic Pancreatitis."—Acute alcoholism or chronic alcoholism with acute episodes is undoubtedly a contributory factor if not a direct etiological factor of acute pancreatitis in man (Table X). Approximately 20 per cent of patients who die with pancreatitis or develop relapsing pancreatitis have a history of alcoholism. Since this incidence of alcoholism in pancreatitis (20 per cent) is higher than that in the general population (4 per cent of adults) it appears that alcoholism predisposes to pancreatitis. Furthermore, 25 per cent of persons dying of acute alcoholic episodes have acute pancreatitis and the serum amylase is elevated in 24 per cent of alcoholic patients and in only 2 per cent of nonalcoholic patients.[103]

TABLE X. RELATION OF ALCOHOL TO ACUTE PANCREATITIS

AUTHOR	NUMBER AUTOPSIES ON ACUTE ALCOHOLICS	NUMBER WITH PANCREATITIS	PER CENT WITH PANCREATITIS
Egdahl[9]	105	17	16
Weiner and Tennant[100]	51	27	53
Myers and Keefer[101]	51	17	33
Clark[48]	150	27	18
Total	357	88	25
	PATIENTS WITH PANCREATITIS	NUMBER OF ALCOHOLICS	PER CENT ALCOHOLICS
Paxton and Payne[5]	307	55	18
Comfort et al.[102]	25*	8**	32**
	NUMBER ALCOHOLICS	NUMBER WITH ELEVATED SERUM AMYLASE	PER CENT SUBCLINICAL PANCREATITIS
Domazalski and Wedge[103]***	51	12	24

*Relapsing pancreatitis

**17, or 68 per cent gave history of liberal drinking, 8 of heavy drinking

***Reported 5 cases of acute hemorrhagic pancreatitis. The serum amylase was elevated in 2 per cent of 50 nonalcoholic controls.

The cause of the pancreatitis associated with alcoholism is uncertain. It has been ascribed to gastroduodenitis[2, 9] which by edema of the papilla of Vater of the pancreatic duct causes obstruction of the pancreas, (b) to vascular congestion and capillary hemorrhage caused by alcohol, and (c) to obstruction of the pancreatic ducts with viscid secretion. The relation of dietary deficiency to this phenomenon has not been studied, as much as the problem deserves.[104, 105] For example, it has been found that a low-protein, high-fat diet and other deficient diets [106-108] including the injection of the amino acid ethionine[109, 110] causes various types of pancreatitis.

In the dog the secretory activity of the pancreas is not significantly affected by large but sublethal amounts of alcohol. Neither is the alcohol concentrated in the pancreatic secretion.[111] We suspect that the acute pancreatitis of the alcoholic is due to a duodenitis which leads to an obstruction of pancreatic outflow and edematous pancreatitis. The vomiting associated with alcoholic episodes may cause rupture of the ducts and account for the severe cases of acute hemorrhagic pancreatitis. (See later paragraph on miscellaneous types of pancreatitis.) A deficient diet may make the pancreas more susceptible.

Traumatic Pancreatitis.—It is well established that trauma to the upper abdomen may cause traumatic pancreatitis which is diagnostically associated with a rise in serum amylase.[75, 112]

The Pancreatitis Associated with Electric Shock.—The mechanism of pancreatitis associated with electric shock is not known and requires further study.[113, 114]

Miscellaneous.—There are a number of miscellaneous causes of pancreatitis which should be mentioned. Numerous cases in which pancreatitis was apparently due to the extension of the inflammation of a duodenal ulcer or diverticulum have been observed. Pancreatitis has been by one of us (G.E.G.) in three children who died with a diabetic acidosis. Pancreatitis has been ascribed to allergy.[115] The repeated ingestion of zinc oxide has caused chronic pancreatitis in cats[116] and dogs.[117]

Pancreatitis develops in rats and dogs on a low-protein, high-fat diet.[104, 106] This may be related to the pancreatitis which occurs in alcoholism, since there is morphologic similarity, and Kirshbaum and Shure[105] found pancreatic fibrosis is 36 per cent of 356 fatal cases of hepatic cirrhosis in persons who were alcoholics.

Complications of Acute Pancreatitis.—The complications of acute pancreatitis in case of survival are: subphrenic abscess, calcification, cyst formation, relapsing pancreatitis, and fibrosis. Gambill and Pugh[6] found that 60 per cent of 39 cases of calcification of the pancreas were associated with a history of relapsing pancreatitis.

Cystic Fibrosis of the Pancreas or Fibrocystic Pancreatitis.—Most known cases of fibrocystic pancreatitis have been found in infancy or early childhood. The disease is characterized chiefly by steatorrhea and bronchitis with subsequent nutritional deficiency and a terminal bronchopneumonia.[118] In recent years two children with this disease have reached the age of 17 years.[119, 120] Hepatic involvement is prominent in the older children.[110, 111] The pulmonary aspect of the disease is not always apparent clinically.[121] This disease probably extends into the adult age in some cases; and if so, steatorrhea, chronic bronchitis, and hepatic insufficiency would be major manifestations. Duodenal drainage with the secretin test is the most reliable way to recognize the condition[122, 123] though the results do not differentiate it from pancreatic fibrosis due to other more common causes in adults.

The cause of the condition is unknown. A deficiency of secretin has been proposed[124] but no deficiency was found by one of us[125] in four children dying of the disease. Vitamin A deficiency has been suggested as a cause, but this is probably a result rather than a cause of the disease. Because of the viscosity of the secretion and the duodenal aspirate in these patients, excessive action of the vagus nerves or a defect in mucin liquefaction has been suggested.[126a] Inadequate protein in the diet of rats and human subjects has been reported to be associated with cystic and fibrotic changes in the pancreas.[126 b-d]

Chronic Relapsing Pancreatitis.—Comfort and his colleagues[102] have described this condition which is characterized by recurrent episodes of pancreatitis which lead to fibrosis and/or calcification[6] with steatorrhea and diarrhea, malnutrition, and/or diabetes.

DIAGNOSIS

Symptoms of Acute or Subacute Pancreatitis.—Pain located in the epigastrium in most cases or in the right or left hypochondrium is a symptom of acute or subacute pancreatitis. The pain in the epigastrium may radiate to the left or to the right. The pain may be mild or very acute or severe and lead to shock. The abdomen is tender, rigid, and distended unless shock occurs. The attack may be accompanied with chills, fever, and leukocytosis. Steatorrhea and a low glucose tolerance may occur.

Symptoms of Chronic Pancreatitis.—Large bulky stools or diarrhea with steatorrhea, malnutrition, and sometimes diabetes, or a diabetic type of blood sugar tolerance curve are symptoms of chronic pancreatitis. Pancreatic calculi may cause attacks of pain.

Acute pancreatic hemorrhagic necrosis stimulates other upper abdominal catastrophes and is not readily differentiated without laboratory tests. The laboratory diagnosis is based principally on finding an elevated serum amylase or lipase, a diabetic type of glucose tolerance curve, or the roentgenographic finding of calculi, of broadening of the duodenal angle, or of a segmental type of ileus. The serum amylase may rise quickly or be normal for the first 8 to 12 hours[10]; the urine amylase lags behind.[5] It may be normal in severe cases. The blood calcium may be low, which is explained as due to the formation of calcium soap in the areas of fat necrosis. The blood calcium and potassium should be determined to direct the therapy.[127]

When pancreatitis is sublethal, it tends to be recurrent, sometimes increasing and sometimes decreasing in the severity of the attacks which may occur over a period of 20 years and have a duration of up to 36 days.[6, 102] The diabetic type of glucose tolerance curve or glycosuria may be transient or progress to mild or severe diabetes as the fibrosis becomes extreme.

In chronic fibrosis or the advanced case of relapsing chronic pancreatitis, in addition to the tests, signs, and symptoms mentioned in the preceding paragraphs, the results of a secretin-duodenal drainage test may be of value.[61, 128] When laboratory facilities are not available, the therapeutic response to adequate doses (8 to 10 Gm. 3 times a day) of pancreatin is decisive.[129, 130]

Many attempts to devise a serum amylase or enzyme test for subacute or relapsing pancreatitis have been made.[131] When the serum amylase and the serum lipase are significantly increased (the latter tending to remain elevated longer), a disturbance of pancreatic function is clearly present. When they are not, then attempts have been made to do something to elevate these enzymes and ascertain the difference between the normal person and one with subacute or chronic pancreatitis. The aim has also been to devise a test more convenient than duodenal drainage. Morphine, Mecholyl, or Urecholine have been given to cause obstruction, and then secretin has been given.[71] A rise occurs in approximately 70 per cent of normal persons. In far advanced fibrosis, the fasting serum amylase values tend to be lower and the rises less. In the presence of acute or subacute pancreatitis, the injection of secretin alone may cause a

rise in serum amylase. This phenomenon deserves further study, since it may prove to be of value in those cases where pancreatitis is suspected though the serum amylase is within the normal range of values.[73]

When a patient has a T tube in place in the common bile duct, it is well to determine whether pancreatic reflux occurs, since if it does, the patient is probably more disposed to develop pancreatitis.

The clinical picture of acute pancreatitis may simulate a number of diseases. The first picture is the textbook description of acute, violent pain, shock, and cyanosis resembling a major coronary occlusion. The second picture simulates that of acute cholecystitis, and is frequently so diagnosed. The third picture resembles an obstruction of the small intestine, and that diagnosis is frequently made. The fourth picture resembles acute gastritis with alcoholism or perforated peptic ulcer. And the fifth is that of a tender mass in the upper abdomen with a history of pain several days previous to the examination.

TREATMENT

The mortality of acute pancreatitis has been markedly reduced in the last 15 years. In 1932, conservative or expectant treatment (4 to 6 days) was advocated[132, 133] and the significance of the serum amylase test in the differential diagnosis of upper abdominal pain began to be more widely recognized.

Acute Pancreatitis.—

Surgical: In the acute severe case surgical intervention is avoided except when there is evidence of suppuration, hemorrhage, effusion, or peritonitis with bile stained fluid; then the abdomen is opened, the fluid removed, the suppuration drained, and any stone in the duct removed; the shock is then treated, and the infection is controlled with penicillin.[3, 5, 132-142]

Medical: To keep secretion at a low ebb and to prevent dehydration, parenteral fluids with glucose are given. In the case of a diabetic glucose tolerance curve or glycosuria, insulin is carefully employed. Gastric lavage and continuous aspiration is used. Ephedrine[139] may be used for shock; it also depresses pancreatic secretion, but in the latter regard ergotamine[140] is superior. Calcium and potassium should be given if the serum level is low.[127]

All agree that morphine, if used for pain, should be used sparingly, because of its effect in promoting contraction of the sphincter of Oddi and probably the sphincter of the pancreatic duct. Demerol may be used guardedly because it possesses some atropine-like action.[142] Barbiturate sedation is preferable. Procaine block from T_4 to T_{10}, or block of the splanchnic nerves is generally recommended for the pain.[5, 14, 138, 143-145] Etamon (tetraethylammonium chloride) (3 to 5 c.c.) has been used intravenously to prevent or abolish the pain,[146] though the rationale of its use is not clear. The nitrites help relieve the pain and relax the sphincters.[137, 146-150] Theophylline has also been used.[151] Atropine will act likewise and will tend to decrease the secretion of enzymes.[5, 14, 152] Magnesium sulfate or oxide given four times a day will help relax the sphincters, decrease edema, and relieve obstruction.[5, 14, 141] Penicillin (300,000 units every 4 to 6 hours) is given to control infection.

Chronic Relapsing Pancreatitis.—

Surgical: Numerous surgical procedures have been tried for the prevention of recurrent attacks of painful pancreatitis.

Cholecystectomy[153, 154] was performed with the idea that it would prevent a concentrated solution of bile salts from refluxing into the pancreatic ducts and would remove the propulsive force of the gall bladder, and temporarily relax the sphincter of Oddi. When this failed, T-tube drainage was used, and like cholecystectomy gave only temporary relief.[136, 154] The sphincter has been dilated with bougies, but this is said to cause injury and scarring.[155] The sphincter has been cut through the bile duct or through the duodenum[57, 61, 156] or a choledochoduodenostomy[157-159] has been performed. The local nerve net about the distal portion of the duct has been sectioned, but one can only expect temporary results from this.[160, 161] A sympathectomy has been performed[144, 162, 163] and the vagi have been sectioned.[163] A splanchnicectomy will section the pain pathway and give relief from pain; it probably has no bearing on the cause of the disease, unless the observation that stimulation of the splanchnic nerves causes pancreatitis in animals is related to the cause of the disease in man.[164] Similarly, vagotomy may have some effect on the cause of the disease (see section of "Parasympathetic Pancreatitis"). Total pancreatectomy has been performed.[159, 165] Subtotal gastrectomy has also been performed with relief of symptoms for at least a short period after the operation.[166] More recently the pancreatic duct has been transplanted into the duodenum to avoid the reflux of bile. This procedure has the disadvantage of permitting reflux of duodenal contents in the duct. A procedure, which has been tried by Bergh, Hay, and Owens,[167] is the double ligation of the duct of Wirsung to prevent reflux and to force the pancreatic juice to flow out through the duct of Santorini. Unfortunately, there is no good way at present to determine uniformly when the accessory duct is patent and connects with the duct of Wirsung.

Section of the sphincter and choledochoduodenostomy are the operations which have been performed most frequently. They undoubtedly have given immediate and temporary relief to many patients. However, adequate data are not available to indicate how permanent the relief is.

In some patients pancreatolithotomy or the removal of a pancreatic cyst is indicated. In others there is evidence of chronic duodenal obstruction which may require surgery.

Fibrocystic Disease.—

Surgical: Fibrocystic disease of the pancreas has been treated surgically by sympathetic denervation of the pancreas and complete sympathectomy on the right side.[168] This was done because it was hypothesized that afferent nervous impulses from the pancreas might reflexly be responsible for the bronchiectasis found in the disease.

Medical: The medical treatment[169] is the same as that for biliary dyskinesia. A diet relatively high in protein and low in fat is used with the idea of promoting bile formation, six small meals being preferable to three larger meals. The

food should be bland and contain soft residue like a late ulcer diet. Bile salts are taken on rising and retiring to keep the bile thin. Magnesium oxide in an amount that does not cause catharsis is taken before retiring and before each meal for its relaxing effect on the sphincter. Belladonna in such quantity as to cause dryness of the mouth may have to be prescribed. Alcohol is forbidden since in the 25 cases studied by Comfort and his colleagues[102] 17 gave a history of alcohol consumption, and 8 of the 17 drank heavily. Adequate evidence of the extent of the value of such a management is lacking.

In the advanced stage of marked fibrosis and deficiency of pancreatic digestion, a deficiency of insulin production may exist and require treatment with insulin. The diarrhea and steatorrhea are benefited by the high-protein, low-fat diet recommended previously, and by the administration of adequate doses of active pancreatin (8-10 Gm.) with each meal. The diet and the pancreatin will correct the malnutrition which is frequently present.[129, 130]

REFERENCES

1. Love, R. J.: Acute Pancreatitis, Lancet **2**: 1262, 1926.
2. Fallis, L. S., and G. Plain: Acute Pancreatitis, SURGERY **5**: 358, 1939.
3. Lewison, E. F.: Acute Pancreatitis: An Etiologic Review and Report of Thirty-five Cases, Arch. Surg. **41**: 1008, 1940.
4. Probstein, J. G., Gray, S. H., Sachar, L. A., and Rindskopf, W. J.: Surgical Implications of Acute Pancreatitis, Arch. Surg. **59**: 189, 1949.
5. Paxton, J. R., and Payne, J. H.: Acute Pancreatitis, Surg., Gynec. & Obst. **86**: 69, 1948.
6. Gambill, E. E., and Pugh, D. G.: Pancreatic Calcification, Arch. Int. Med. **81**: 301, 1948.
7. McWhorter, G. L.: Acute Pancreatitis, Arch. Surg. **25**: 958, 1932.
8. Guleke, N.: Demonstration einer experimentell Gewonnenen pankreasnekrose, Berl. klin. Wchnschr. **41**: 682, 1904.
9. Egdahl, A.: A Review of One Hundred and Five Reported Cases of Acute Pancreatitis With Special Reference to Etiology and Report of Two Cases, Bull. Johns Hopkins Hosp. **18**: 130, 1907.
10. McCorkle, H., and Goldman, L.: Clinical Significance of Serum Amylase Test in Diagnosis of Acute Pancreatitis, Surg., Gynec. & Obst. **74**: 439, 1942.
11. Molander, D. W., and Bell, E. T.: Relation of Cholelithiasis to Acute Hemorrhagic Pancreatitis, Arch. Path. **41**: 17, 1946.
12. (a) Deaver, J. B.: A Clinical Study of Pancreatitis, Ann. Clin. Med. **2**: 1, 1924.
    (b) Judd, E. S.: Relation of the Liver and Pancreas to Infection of the Gall Bladder, J. A. M. A. **77**: 197, 1921.
13. Kaufman, M.: Experimental Study of the Lymphatic Theory of Pancreatitis: Etiology and Pathogenesis, Surg., Gynec. & Obst. **44**: 15, 1927.
14. Tejerina-Fotheringham, W.: Acute Pancreatitis, Gastroenterology **10**: 687, 1948.
15. Dragstedt, L. R., Haymond, H. E., Ellis, J. C.: Pathogenesis of Acute Pancreatitis, Arch. Surg. **28**: 232, 1934.
16. (a) Rich, A. R., and Duff, G. L.: Experimental and Pathological Studies on the Pathogenesis of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **58**: 212, 1936.
    (b) Northrop, J. H.: Crystalline Enzymes. The Chemistry of Pepsin, Trypsin and Bacteriophage, New York, 1939, Columbia University Press.
17. Ivy, A. C.: Unpublished Observations.
18. Wangensteen, O. H., Leven, N. L., and Manson, M. N.: Acute Pancreatitis: Experimental and Clinical Study With Special Reference to Significance to Biliary Tract Factor, Arch. Surg. **23**: 47, 1931.
19. Kodama, S.: Lymphatics of Extrahepatic Biliary Passages, Surg., Gynec. & Obst. **43**: 140, 1926.
20. Brahdy, M. B., and Scheffer, I. H.: Pancreatitis Complicating Mumps, Am. J. M. Sc. **181**: 255, 1931.
21. Applebaum, I. L.: Serum Amylase in Mumps, Ann. Int. Med. **21**: 35, 1944.
22. Poppel, M. H., and Bacon, G.: The Roentgen Manifestations of Pancreatitis Complicating Mumps, Am. J. Roentgenol. **61**: 219, 1949.
23. Bass, L., and Tudor, R. B.: The Serum Amylase Levels in Mumps, Lancet **69**: 188, 1949.

24. Caudell, S., and Wheelock, M. C.: Serum Amylase and Serum Lipase in Mumps, Ann. Ann. Int. Med. **25**: 88, 1946.
25. Kreilkamp, B. L., and Boyden, E. A.: Variability in Composition of Sphincter of Oddi, Anat. Rec. **76**: 485, 1940.
26. Opie, E. L.: Disease of the Pancreas, ed. 2, Philadelphia, 1910, J. B. Lippincott Co.
27. Mann, F. C., and Giordano, A. S.: The Bile Factor in Pancreatitis, Arch. Surg. **6**: 1, 1923.
28. Baldwin, W. M.: The Pancreatic Ducts in Man, Together With a Study of the Microscopic Study of the Minor Pancreatic Papilla, Anat. Rec. **5**: 197, 1911.
29. Belou, P.: Anatomia de los conductos biliares y de la arteria cistica, Buenos Aires, 1915, Imp. "Oceana."
30. Rienhoff, W. F. Jr., and Pickrell, K. L.: Pancreatitis, Arch. Surg. **51**: 205, 1945.
31. Millbourn, E.: On the Excretory Ducts of the Pancreas in Man, With Special Reference to Their Relations to Each Other, to the Common Bile Duct and to the Duodenum, Acta anat. **9**: 1, 1950.
32. Hjorth, E.: Contributions to the Knowledge of Pancreatic Reflux as an Etiologic Factor in Chronic Affections of the Gall Bladder, Acta Chir. Scandinav. (supp. 134) **96**: 1947.
33. Cameron, A. L., and Noble, J. F.: Reflux of Bile Up the Duct of Wirsung Caused by an Impacted Biliary Calculus, J. A. M. A. **82**: 1410, 1924.
34. Howard, J., and Jones, R.: The Anatomy of the Pancreatic Ducts: The Etiology of Acute Pancreatitis, Am. J. M. Sc. **214**: 617, 1947.
35. Mehnen, H.: Die Bedeutung der Mündungsverhältnisse von Gallen- und Pankreasgang für die Entstehung der Gallensteine, Arch. f. klin. Chir. **192**: 559, 1938.
36. Schirmer, A. M.: Beitrag zur Geschichte und Anatomie des Pankreas, Basel, 1893, Reinhardt.
37. Ruge, E.: Beiträge zur Chirurgischen Anatomie der Grossen Gallenwege (Ductus hepaticus, choledochus und pancreaticus), Arch. f. klin. Chir., Berl. **87**: 47, 1908.
38. Hunt, H. B., Hicken, N. F., and Best, R. R.: Exploration of Biliary Ducts by Cholangiography During and Following Operation, Am. J. Roentgenol. **38**: 542, 1937.
39. Robins, S. A., and Hermanson, L.: Cholangiography; Modified Technique for X-ray Visualization of Bile Ducts During Operation, Surg., Gynec. & Obst. **62**: 684, 1936.
40. Colp, R., and Doubilet, H.: Operative Incidence of Pancreatic Reflux in Cholelithiasis, SURGERY **4**: 837, 1938.
41. Leven, N. L.: Reflux Into the Major Pancreatic Duct During Cholangiography, Proc. Soc. Exper. Biol. & Med. **38**: 808, 1938.
42. Howell, C. W., and Bergh, G. S.: Pancreatic Duct Filling During Cholangiography: Its Effect Upon Serum Amylase Levels, Gastroenterology **16**: 309, 1950.
43. Liedberg, N.: Erfahrungen mit primärer Cholangiographie unter besonderer Berücksichtigung etwaiger Schadigungen des Pankreas, Acta chir. Scandinav. **85**: 261, 1941.
44. Rudstrom, F. P.: Cholangiographie während der Operation; Technik, röntgenologie und Bedeutung für die Praxis, Acta chir. Scandinav. (supp. 97) **91**: 1-131, 1944.
45. Hulten, O.: Über die Topographie des Gallen- und Pankreasganges unter Berücksichtigung postoperativer Pankreasfisteln, Deutsche Ztschr. f. Chir. **252**: 41, 1939.
46. Stenström, B.: Uber cholangiographie, Acta radiol. **21**: 549, 1940.
47. Yotuyanagi, S.: Metaplasie des Ausführungsgangsepithels im menschlichen Pankreas, Mitt. u. allg. Path. u. path. Anat. **9**: 403, 1937.
48. Clark, E.: Pancreatitis in Acute and Chronic Alcoholism, Am. J. Digest. Dis. **9**: 428, 1942.
49. Schmieden, V., and Sebening, W.: Chirgurie des Pankreas, Arch. f. klin. Chir. **148**: 319, 1927.
50. Smyth, C. J.: Etiology of Acute Hemorrhagic Pancreatitis, With Special Reference to Vascular Factors, Arch. Path. **30**: 651, 1940.
51. Opie, E. L.: The Etiology of Acute Hemorrhagic Pancreatitis, Bull. Johns Hopkins Hosp. **12**: 182, 1901.
52. Duncan, N. A.: Pancreatitis Due to Ascariasis, Brit. M. J. **1**: 905, 1948.
53. Rigdon, R. H.: Obstruction of Ampulla Due to a Tumor and Acute Hemorrhagic Pancreatitis, Am. J. Clin. Path. **18**: 387, 1948.
54. Rienhoff, W. F. Jr., and Lewis, D.: Surgical Affections of Pancreas Met With in Johns Hopkins Hospital From 1889 to 1932, Including Report of Case of Adenoma of Islands of Langerhans, and Case of Pancreatolithiasis, Bull. Johns Hopkins Hosp. **54**: 386, 1934.
55. Weiner, J.: The Relation of Cholelithiasis to Acute Pancreatitis, N. York M. J. **77**: 889, 1903.
56. Baló, J., and Ballon, H. C.: Effects of Retention of Pancreatic Secretion, Surg., Gynec. & Obst. **48**: 1, 1929.
57. Archibald, E.: Experimental Production of Pancreatitis in Animals as a Result of Resistance of Common Duct Sphincter, Surg., Gynec. & Obst. **28**: 529, 1919.

58. Ivy, A. C., and Sandblom, P.: Biliary Dyskinesia, Bull. Johns Hopkins Hosp. **54**: 386, 1934.
59. Layne, J. A., and Bergh, G. S.: Experimental Study of Pain in Human Biliary Tract Induced by Spasm of Sphincter of Oddi, Surg., Gynec. & Obst. **70**: 18, 1940.
60. Ryan, J. D., Doubilet, H., and Mulholland, J. H.: Observations on Biliary-Pancreatic Dynamics in Normal Human, Gastroenterology **13**: 1, 1949.
61. (a) Doubilet, H., and Mulholland, J. H.: The Surgical Treatment of Recurrent Acute Pancreatitis by Endocholedochal Sphincterotomy, Surg., Gynec. & Obst. **86**: 295, 1948.
(b) Recurrent Acute Pancreatitis: Observation on Etiology and Surgical Treatment, Ann. Surg. **128**: 609, 1948.
62. Doubilet, H.: Pancreatic Reflux Deliberately Produced, Surg., Gynec. & Obst. **84**: 710, 1947.
63. Ivy, A. C.: Motor Dysfunction of the Biliary Tract: An Analytical and Critical Consideration, Am. J. Roentgenol. **57**: 1, 1947.
64. Lium, R., and Maddock, S.: Etiology of Acute Pancreatitis, SURGERY **24**: 593, 1948.
65. Popper, H. L.: Enzyme Studies in Edema of the Pancreas and Acute Pancreatitis, SURGERY **7**: 566, 1940.
66. Keyl, R.: Ueber die Beziehungen des Santorinischen Ganges zum Zwölffingerdarm und zum Wirsungschen gang, Morphol. Jahrb., Leipz. **55**: 345, 1925.
67. Nabatoff, R. A.: Relationship of Pancreatic Duct Obstruction and Dilatation to Fat Necrosis of Pancreas, J. Mt. Sinai Hosp. **15**: 139, 1948.
68. Popper, H. L., Necheles, H., Russell, K. C.: Transition of Pancreatic Edema Into Pancreatic Necrosis, Surg., Gynec. & Obst. **87**: 79, 1948.
69. Lagerlof, H.: Normal Esterases and Pancreatic Lipase in the Blood, Acta med. Scandinav. **120**: 407, 1945.
70. Howard, J. M., Smith, A. K., and Peters, J. J.: Acute Pancreatitis: Pathways of Enzymes Into the Blood Stream, SURGERY **26**: 161, 1949.
71. Burke, J. O., Plummer, K., and Bradford, S.: Serum Amylase Response to Morphine, Mecholyl, and Secretin as a Test of Pancreatic Function, Gastroenterology **15**: 699, 1950.
72. Myhre, J. G., Nesbitt, S., Hurly, J. T.: A Study of Serum Amylase and Lipase, Gastroenterology **13**: 127, 1949.
73. Lopusniak, M. S., and Bockus, H. L.: Study of Pancreatic Serum Enzymes Following Secretin Injection in Pancreatic Affections, Gastroenterology **16**: 294, 1950.
74. Foged, J.: The Diagnostic Value of Urine Diastase, Am. J. Surg. **27**: 439, 1935.
75. Naffziger, H. C., and McCorkle, H. J.: The Recognition and Management of Acute Trauma to the Pancreas, With Particular Reference to the Use of the Serum Amylase Test, Ann. Surg. **118**: 594, 1943.
76. Bockus, H. L.: Postgraduate Gastroenterology, Philadelphia, 1950, W. B. Saunders Company.
77. Wang, C. C., Wang, K. J., and Grossman, M. I.: Effects of Ligation of the Pancreatic Duct Upon the Action of Secretin and Pancreozymin in Rabbits With Correlated Histological Study, Am. J. Physiol. **160**: 115, 1950.
78. Popper, H. L., and Necheles, H.: Pathways of Enzymes Into the Blood in Acute Damage of the Pancreas, Proc. Soc. Exper. Biol. & Med. **43**: 220, 1940.
79. Popper, H. L.: Diffusion of Pancreatic Enzymes Through the Intestinal Wall in Ileus, SURGERY **7**: 571, 1940.
80. Walzel, P.: Zur Diagnostik und Therapie der akuten Pankreasnekrose, Wien. klin. Wchnschr. **42**: 14, 1929.
81. Ireneus, C.: Experimental Bile Pancreatitis, Arch. Surg. **42**: 126, 1941.
82. Reid, Stephen: The Effect of Pancreatic Juice on the Gallbladder, Surg., Gynec. & Obst. **89**: 160, 1949.
83. (a) Nordman, O.: Experimente und klinische Betrachtungen über die Zusammen hänge Zwischen acuter Pankreatitis und Erkrankungen der Gallenblase, Arch. f. klin. Chir. **102**: 66, 1913.
(b) Nordman, O.: Neuere Anschaungen über die akute Pankreasnekrose und ihre Behandlung, Arch. f. klin. Chir. **193**: 370, 1938.
84. Bisgard, J. D., and Baker, C. P.: Studies Relating to the Pathogenesis of Cholecystitis, Cholelithiasis, and Acute Pancreatitis, Ann. Surg. **112**: 1006, 1940.
85. Popper, H. L.: Etiology of Acute Pancreatitis, Am. J. Digest. Dis. **9**: 186, 1942.
86. Dardinski, V. J.: Hemorrhagic Pancreatitis: Report of Two Cases in Which Gallstones Could Not Be Considered Essential Etiological Factors, Am. J. Path. **7**: 169, 1931.
87. Johnstone, O. P.: Four Cases of Hemorrhagic Pancreatitis in Which the Common Bile Duct and Pancreatic Ducts Had Separate Openings, Colorado M. J. **4**: 93, 1907.
88. New C. F.: Acute Hemorrhagic Pancreatitis, J. A. M. A. **45**: 2011, 1905.
89. Simkins, S.: Variations in Pancreatic Ducts and Minor Duodenal Papilla, Am. J. M. Sc. **182**: 626, 1931.

90. Babkin, B. P.: Einige Grundeigenschaften der Fermente des Pankreassaftes, Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs. **1**: 98, 1906.
91. Crittenden, P. J., and Ivy, A. C.: The Nervous Control of Pancreatic Secretion in the Dog, Am. J. Physiol. **119**: 724, 1937.
92. Effront, J.: Biochemical Catalysts in Life and Industry, Trans. by Prescott, S. C., New York, 1917, John Wiley & Sons, Inc.
93. Ivy, A. C., Grossman, M. I., and Bachrach, W. H.: Peptic Ulcer, Philadelphia, 1950, The Blakiston Company.
94. Gibbs, G. E., and Ivy, A. C.: Early Histological Changes in the Pancreas Following Obstruction of the Pancreatic Ducts in the Dog, Proc. Soc. Exper. Biol. & Med. **77**: 251, 1951.
95. Tucker, A. L.: Inhibition of Pancreatic Vacuolization, J. Pharmacol. & Exper. Therap. **92**: 421, 1948.
96. Lium, R., Portsmouth, N. H., and Maddock, S.: Etiology of Acute Pancreatitis, SURGERY **24**: 593, 1948.
97. Coffey, R. J.: Diseases of Pancreas; Acute Diseases, M. Ann. District of Columbia **11**: 131, 1942.
98. Werner, J., Simon, M. A., and Hoff, H. E.: Production of Acute Pancreatitis in Dogs by the Administration of Mecholyl, Gastroenterology **15**: 125, 1950.
99. Farber, S.: The Experimental Production of Achylia Pancreatica, Am. J. Dis. Child. **64**: 593, 1942.
100. Weiner, H. A., and Tennant, R.: A Statistical Study of Acute Hemorrhagic Pancreatitis, Am. J. M. Sc. **196**: 167, 1938.
101. Myers, W. K., and Keefer, C. S.: Acute Pancreatic Necrosis in Acute and Chronic Alcoholism, New England M. J. **210**: 1376, 1934.
102. Comfort, M. W., Gambill, E. E., and Baggenstoss, A. H.: Chronic Relapsing Pancreatitis, Gastroenterology **6**: 376, 1946.
103. Domazalski, C. A., and Wedge, B. M.: Elevated Serum Amylase in Alcoholics, Am. J. Clin. Path. **18**: 43, 1948.
104. Lindsay, S., Enterman C., and Chaikoff, I. L.: Pancreatitis Accompanying Hepatic Disease in Dogs Fed a High Fat, Low Protein Diet, Arch. Path. **45**: 635, 1948.
105. Kirshbaum, J. D., and Shure, N.: Alcoholic Cirrhosis of Liver, Clinical and Pathologic Study of 356 Fatal Cases Selected From 12,267 Necropsies, J. Lab. & Clin. Med. **28**: 721, 1943.
106. Grossman, M. I., Greengard, H., and Ivy, A. C.: The Effect of Dietary Composition on Pancreatic Enzymes, Am. J. Physiol. **138**: 676, 1943.
107. Gillman, T., and Gillman, J.: Powdered Stomach in Treatment of Fatty Liver and Other Manifestations of Infantile Pellagra, Arch. Int. Med. **76**: 63, 1945.
108. Davies, J. N. P.: The Essential Pathology of Kwashiorkor, Lancet **1**: 317, 1948.
109. Goldberg, R. C., Chaikoff, I. L., Doge, A. H.: Destruction of Pancreatic Acinar Tissue by Ethionine, Proc. Soc. Exper. Biol. & Med. **74**: 869, 1950.
110. (a) Farber, E., and Popper, H.: Production of Acute Pancreatitis With Ethionine and Its Prevention With Methionine, Proc. Soc. Exper. Biol. & Med. **74**: 836, 1950.
(b) Almeida, A. L., Pine, B. W., and Grossman, M. I.: Unpublished Studies.
111. Barroso, E. J.: Some Effects of Alcohol on Pancreatic Secretion, M. S. Thesis, Northwestern University Medical School, June, 1947.
112. Stern, E. J.: Traumatic Injuries to the Pancreas, Am. J. Surg. **8**: 58, 1930.
113. Glazer, A. M.: Pancreatic Necrosis in Electric Shock, Arch. Path. **39**: 9, 1945.
114. Sirolli, M.: Sulla patologica della morte de elettricita (Picerche anatomopathologische e fisiopatologiche), Arch. ital. chir. **33**: 333, 1933.
115. Shaffer, J.: Allergic Pancreatitis, Permanente Found. M. Bull. **6**: 204, 1948.
116. Drinker, K. R., Thompson, P. K., and Marsh, M.: An Investigation of the Effect of Long Continued Ingestion of Zinc, in the Form of Zinc Oxide, by Cats and Dogs, Am. J. Physiol. **80**: 31, 1927.
117. Ivy A. C.: Unpublished Observations.
118. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease, Am. J. Dis. Child. **56**: 344, 1938.
119. Kohl, H. W.: Fibrocystic Disease of the Pancreas, Arizona Med. **5**: 47, 1948.
120. Pugsley, H. E., and Spence, P. M.: A Case of Cystic Fibrosis of the Pancreas Associated With Chronic Pulmonary Disease and Cirrhosis of the Liver, Ann. Int. Med. **30**: 1262, 1949.
121. Gibbs, G. E.: The Effect of Pancreatin on Plasma Vitamin A Curves in the Celiac Syndrome, Pediatrics **6**: 593, 1950.
122. Gibbs, G. E.: Secretin Tests With the Bilumen Gastroduodenal Drainage in Infants and Children, Pediatrics **5**: 941, 1950.
123. Dreiling, D. A., and Hollander F.: Studies in Pancreatic Function. I. Preliminary Series of Clinical Studies With the Secretin Test, Gastroenterology **11**: 714, 1948.

124. Baggenstoss, A. H., Power, M. H., and Grindlay, J. H.: The Extraction of Secretin From the Intestine of Man: Absence of Secretin in a Case of Fibrocystic Disease of the Pancrease, Gastroenterology **11:** 208, 1948.
125. Gibbs, G. E., and Gershbein, L. L.: Presence of Secretin in Systic Fibrosis of the Pancreas, Proc. Soc. Exper. Biol. & Med. **74:** 336, 1950.
126. (a) Farber, S.: Some Organic Digestive Disturbances in Early Life, J. Michigan M. Soc. **44:** 587, 1945.
(b) Veghelyi, P. V., Kemeny, T. T., and Sos, J.: Cystic Change in the Pancreas. Its Experimental Production, Am. J. Dis. Child. **79:** 65, 1950.
(c) Veghelyi, P. V., Kemeny, T. T., Pozsonyi, J., and Sos, J.: Dietary Lesions of the Pancreas, Am. J. Dis. Child. **79:** 658, 1950.
(d) Gillman, J., Gilbert, C., and Gillman, T.: Bantu Salivary Glands in Chronic Malnutrition, South African J. M. Sc. **12:** 99, 1947.
127. Edmondson, H. A., and Berne, C. J.: Calcium Changes in Acute Pancreatic Necrosis, Surg., Gynec. & Obst. **79:** 240, 1944.
128. (a) Dornberger, G. R., Comfort, M. W., Wollaeger, E. E., and Power, M. H.: Pancreatic Function as Measured by Analysis of Duodenal Contents Before and After Stimulation of Secretin, Gastroenterology **11:** 701, 1948.
(b) Total Fecal Solids, Fat and Nitrogen: A Study of Patients With Chronic Relapsing Pancreatitis, Gastroenterology **11:** 691, 1948.
129. Beazell, J. M., Schmidt, C. R., and Ivy, A. C.: The Diagnosis and Treatment of Achylia Pancreatica, J. A. M. A. **116:** 2735, 1941.
130. Pratt, J. H.: Diagnosis of Pancreatic Disease, N. Y. State J. Med. **43:** 1847, 1943.
131. Johnson, T. A., and Bockus, H. L.: Diagnostic Significance of Determinations of Serum Lipase, Arch. Int. Med. **66:** 62, 1940.
132. deTakats, G., MacKenzie, W. C.: Acute Pancreatic Necrosis and Its Sequelae, Critical Study of 30 Cases, Ann. Surg. **96:** 418, 1932.
133. Wangensteen, O. H.: Acute Pancreatic Necrosis With Comments on Diagnosis and Therapy, Minnesota Med. **15:** 201, 1932.
134. Whipple, G. H., and Goodpasture, E. W.: Acute Hemorrhagic Pancreatitis, Surg., Gynec. & Obst. **17:** 541, 1913.
135. Cooke, J. V., and Whipple, G. H.: Protease Intoxications and Injury of Body Protein, J. Exper. Med. **28:** 223, 1918.
136. Cole, W. H.: Treatment of Acute Pancreatitis: Collective Review, Internat. Abst. Surg. **67:** 31, 1938.
137. Elman, R.: Surgical Aspects of Acute Pancreatitis, J. A. M. A. **118:** 1265, 1942.
138. Pearson, S., and Lungren, J. C.: Relief of Pain in Acute Pancreatitis, Ann. West Med. & Surg. **2:** 550, 1948.
139. Craft, C. B.: The Effect of Ephedrine on Pancreatic Secretin: Method for the Management of Patients Having a Pancreatic Fistula, SURGERY **4:** 64, 1938.
140. Roback, R. A.: The Effect of Sympathomimetic Amines and Related Compounds on Pancreatic Secretion, M. S., Thesis, Northwestern University, 1942.
141. Lium, R.: The Diagnosis and Conservative Treatment of Acute Pancreatitis, New England M. J. **219:** 881, 1938.
142. Bockus, H. L., and Raffensperger, E. C.: Acute Pancreatitis, New York State J. Med. **48:** 2252, 1948.
143. Popper, H. L.: Paravertebrale injektion bei pankreatitis, Zentralbl. Chir. **60:** 2050, 1933.
144. DeTakats, G., and Walter, L. E.: Treatment of Pancreatic Pain by Splanchnic Nerve Section, Surg., Gynec. & Obst. **85:** 742, 1947.
145. Morton, J. J.: Acute Pancreatitis, SURGERY **17:** 475, 1945.
146. Cunha, F.: Diagnosis and Treatment of Pancreatic Disease, Am. J. Surg. **58:** 16, 1942.
147. Elman, R.: A Note on the Use of Nitroglycerine in the Immediate Treatment of Acute Non-hemorrhagic Pancreatitis, Am. J. Digest. Dis. **6:** 474, 1939.
148. Best, R. R., and Hicken, N. F.: Cholangiographic Demonstration of Biliary Dyssynergia and Other Obstructive Lesions of Gall Bladder and Bile Ducts, J. A. M. A. **107:** 1615, 1936.
149. McGowan, J. M., Butsch, W. L., and Walters, W.: Pressure in Common Bile Duct of Man; Its Relation to Pain Following Cholecystectomy, J. A. M. A. **106:** 2227, 1936.
150. Doubilet, H., and Colp, R.: Resistance of Sphincter of Oddi in Human, Surg., Gynec. & Obst. **64:** 622, 1937.
151. Alvare, L. R.: Theophylline Ethylenediamine in the Control of Acute Cases of Hemorrhagic Pancreatitis, With Deferring of Surgical Therapy, Vida nueva, **60:** 1, 1947.
152. Lueth, H. C.: Studies on the Flow of Bile Into the Duodenum and the Existence of the Sphincter of Oddi, Am. J. Physiol. **99:** 237, 1931.
153. Judd, E. S.: Recurrence of Symptoms Following Operations on the Biliary Tract, Ann. Surg. **67:** 473, 1918.
154. Wangensteen, O. H., Leven, N. L., and Manson, M. H.: Acute Pancreatitis (Pancreatic Necrosis); Experimental and Clinical Study, With Special Reference to Significance of Biliary Tract Factor, Arch. Surg. **23:** 47, 1931.

155. Zollinger, R., Brauch, C. D., and Bailey, O. T.: Instrumental Dilation of the Papilla of Vater, Surg., Gynec. & Obst. **66**: 100, 1938.
156. Archibald, E., and Gibbons, E. C.: Further Data Concerning Experimental Production of Pancreatitis, Tr. Am. S. A. **39**: 96, 1921.
157. Waugh, J. M.: Chronic Relapsing Pancreatitis: Surgical Management, Proc. Staff Meet., Mayo Clin. **22**: 558, 1947.
158. Walters, W., Gray, H. K., and Priestley, J. T.: Annual Report on Surgery of Biliary System and Pancreas for 1946, Proc. Staff Meet., Mayo Clin. **23**: 40, 1948.
159. Maimon, S. N., Kirsner, J. B., and Palmer, W. L.: Chronic Recurrent Pancreatitis; Clinical Study of 20 Cases, Arch. Int. Med. **81**: 56, 1948.
160. Reich, H.: Choledochal Denervation: A New Procedure for the Relief of Biliary Dyskinesia, Surg., Gynec. & Obst. **71**: 39, 1940.
161. Lagerlof, H.: A Choledochal Denervation in Biliary Dyskinesia, Acta chir. Scandinav. **95**: 297, 1947.
162. Mallet-Guy, P., and de Beaujeu, Junbert: Unilateral Splanchnicectomy for Digestive Indications (Megadolicho-colon, Atony of Biliary Tract and Chronic Pancreatitis); Results in 103 Cases, Wien. Acad. de chir. **73**: 189, 1947.
163. Reinhoff, W. E., Jr., and Baker, B. M.: Pancreolithiasis and Chronic Pancreatitis: Preliminary Report of a Case of Apparently Successful Treatment by Transthoracic Sympathectomy and Vagectomy, J. A. M. A. **134**: 20, 1946.
164. Mallet-Guy, P., Feroldi, J., and Reboul, E.: Researches experimentales sur la pathogeine des pancréatites Aignës; leur provocation par l'excitation du nerf splanchnique gavche, Lyon chir. **44**: 281, 1949.
165. Child, C. G.: Radical One-Stage Pancreaticoduodenectomy, SURGERY **23**: 492, 1948.
166. Richman, A., and Colp, R.: Subtotal Gastrectomy in the Treatment of Recurrent Pancreatitis, J. Mt. Sinai Hosp. **15**: 132, 1948.
167. Bergh, G. S., Hay, Lyle, and Owens, F.: Personal communication.
168. Ayers, W., Stovens, D., and Ochsner, A.: Fibrocystic Disease of the Pancreas, J. A. M. A. **142**: 7, 1950.

Book Reviews

Clinical Nutrition. Edited by Normal Jalliffe, Fredrick Tisdale, and Paul Cannon, for the Food and Nutrition Board of the National Research Council, Ed. 1. Pp. 925, with 127 illustrations. Price, $12.00. New York, 1950, Paul B. Hoeber, Inc. $12.00.

Nutritional problems as they relate to medical practice have attracted the attention of all levels of medical science. In recent years, tremendous strides have been made toward a sounder understanding of the altered physiology in nutritional disturbances, and a more specific and rational approach to therapy of these alterations has evolved. This volume, prepared under the direction of the editors for the Food and Nutrition Board of the National Research Council, presents the viewpoints of thirty-six contributors, each an active investigator in the field which he discusses.

The volume is well organized into four parts, each subdivided into chapters with (1) diagrams of nutritional deficiency, (2) the nutritional elements, (3) therapy and prevention, and (4) a valuable appendix containing recommended dietary allowances, tables for calculating diets, dietary patterns, and ideal weight tables for men and women. Investigative techniques, methods, and tracer element studiesd are discussed in addition to other laboratory and clinical findings and studies. The clinical aspects of nutritional disturbances are capably described and vividly illustrated with many colored reproductions as well as other photographs, charts, and tables.

This volume presents, in a clear, concise manner, current knowledge in the field of nutrition and should prove extremely useful to practicing physicians as well as a reference source for students, specialists, and teachers.

Essentials of Urology. By J. C. Ainsworth-Davis M.C., B.Ch. (Cant.), F.R.C.S. (Eng. and Edin.), Urological Surgeon, The Bollingbroke Hospital, London, Visiting Urologist, Kettering and District General Hospital and the Lord Mayor Treloar's Hospital, Alton, Hon. Consulting Urologist, Royal Waterloo Hospital, London, Late Wing-Commander i/c Surgical Division, Royal Air Force Medical Service, Secretary to Council, Royal Society of Medicine. Springfield, Ill., 1950, Charles C Thomas, Publisher.

This textbook presents a well-organized account of the fundamentals of Urology. The subject matter is clearly presented and is easy to read. The text is well illustrated. The terminology employed by this English author may occasionally confuse the medical student in the United States, but not the experienced Urologist. The names used for reagents and medications (proprietary) may also confuse the reader.

The author places undue emphasis on the dangers of sudden emptying of the chronically distended urinary bladder. His reference to cystine calculi throwing the best radiographic shadow of all urinary calculi is obviously an error. His discussion of plastic procedures for the relief of obstruction at the ureteropelvic junction is limited to the von Lichtenberg procedure. One gathers that nephrectomy for hydronephrosis is performed more often in England than in this country.

The student will find in the discussion of the management of vesical neck obstruction that the English place more emphasis on the standard open surgical procedures. Transurethral prostatic resection (perurethral resection) is employed for relief of obstruction due to contracture of the vesical neck, small median lobe enlargement, and prostatic carcinoma. In this country, particularly in the Middle West, the majority of vesical neck obstructions are dealt with by transurethral resection.

The section on retropubic prostatectomy is well presented and is taken almost completely from Millin's book, *Retropubic Urinary Surgery.*

One might expect that a textbook published in 1950 would contain a more complete discussion of the use of antibiotics and chemotherapeutic agents in the management of infections in the urinary tract.

The Urologist will find this textbook interesting because the British viewpoint on certain aspects of this specialty is often quite different. Not necessarily fundamentally different, but just different. It is a good source of reference for the urologic fundamentals, but detailed information on any specific subject cannot be found here.

The student will find this a good reference textbook to supplement his classroom lectures and demonstrations. Contemporary American textbooks of Urology will serve student needs a bit better, but knowledge of the subject can be broadened by having access to this textbook.

The physician in general practice will find this textbook valuable as a ready source of reference. The illustrations are clear and simple. The author lists forty-one references, twenty-six of which are to the current urological literature, the balance to standard textbooks of Urology, monographs, and personal communications.

Color Atlas of Morphologic Hematology With a Guide to Clinical Interpretation. By Geneva A. Daland, B.S., Edited by Thomas Hale Ham, M.D., Pp. 74, with 14 illustrations by Etta Piotti. Cambridge, Mass. Harvard University Press.

As stated in the foreword, the purpose of this Atlas is to furnish a guide for reference in the study of peripheral blood stained with Wright's stain. This purpose is accomplished most successfully.

The Atlas is composed of twenty-one sections. The first four sections deal with the value and limitations of the blood film in diagnosis, preparation of blood films, and general characteristics of the formed elements of the blood stained with Wright's stain. Recognition of the red-white and thrombocytic-cell series is discussed in the next three sections. The remainder deals with leukemias, anemias, and infectious mononucleosis. In this latter section, data on patients are presented along with representative plates. The morphologic aspects and clinical interpretations are emphasized.

This volume is of practical value to the student, technician, and physician. The information is presented in a clear and concise manner. The illustrations and descriptive morphology are both well done. The clinical interpretations will be of great help to physicians and particularly to students.

Lehrbuch der Roentgendiagnostik. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. Vol. 1, Sections 1, 2, and 4. Ed. 5. Pp. 1920, with 2,676 illustrations. Stuttgart, 1950, Georg Thieme. Agents in U.S.: Grune and Stratton, New York. $36.00.

This is the fifth edition of a well-known textbook of roentgen diagnosis which has been a standard reference work upon the European Continent for many years. The general organization of the text matter follows somewhat the lines developed in the previous editions. Volume I concerns the skeleton. The first section or portion of this volume consists of 426 pages and includes 507 figures and 58 tables. The work is opened with a discussion upon fundamentals of the theory of roentgenograms. This discussion is followed by protective measures used in roentgen departments and a discussion of general methods used in diagnostic roentgenology.

The roentgen diagnosis of the skeleton is introduced by a discussion of the general roentgen symptomatology or findings of the normal skeleton followed by the type of roentgen signs noted in the pathologic skeleton. Circulatory changes, infarcts, and bone injuries caused by physical agents are considered. There is a fairly brief discussion of the so-called alarm syndrome in bones. Considerable space is then given to fractures, including the mechanism of fracture, the type of roentgen signs seen in the examination of fracture cases, the study of fracture healing by the roentgen methods, and the roentgenographic control of different treatment methods as the cases are followed.

Section 2 continues with the roentgen examination of the skeleton. Aseptic necrosis in the epiphyses, apophyses, and small bones are discussed. A largely new section takes up the so-called toxic osteopathies. Exogenous poisons discussed include phosphorus, strontium, lead, bismuth, cadmium, and chlorine. The endogenous form of toxic osteopathy is discussed under the heading of "Osteopathy Hypertrophicans Toxica." There is a fairly comprehensive discussion of inflammatory bone diseases. The authors include osteoid osteoma, eosinophilic granuloma, and the cortical hyperostosis of Caffey in this particular discussion. Another important feature in this section is the discussion on hereditary bone diseases by Cocchi. Over 200 pages are devoted to this discussion, which is approximately doubled from the old edition, and which is probably one of the most thorough presentations in radiologic literature.

Section 4 completes the discussion of the skeleton and includes many aspects of soft tissue roentgenography. This section consists of 513 pages, with 674 figures and 30 tables. The first portion deals with the vertebral column and includes good general discussion of most of the variations, anomalies, and diseases involving the spine. A section on myelography is included.

The roentgen diagnosis of the skull is divided into the findings on plain roentgenograms, pneumography, cerebral angiography, the temporal bone, nose and sinuses, the orbit and its contents, and studies of the teeth and jaw. The presentation on cerebral angiography is considerably expanded, since the procedure is used much more frequently now than at the time of previous editions of this work. Numerous reproductions and diagrammatic sketches are included in this discussion.

Soft tissue roentgenographic studies are then presented, including roentgen signs noted in muscles, ligaments, subcutaneous tissues, blood vessels, breast, and salivary glands. Arteriography and venography are discussed more thoroughly than in previous editions and several good reproductions are included.

Foreign bodies and their localization is discussed by Zuppinger. Different methods and the principles involved are presented.

The last portion of the first volume on the skeleton is concerned with differential diagnosis of bone diseases. A few pages are devoted to differential diagnosis from the topographic point of view. This is followed by so-called roentgen sketches of the skeleton in which various diseases are depicted according to the relative frequency with which the condition affects various parts of the skeleton.

The authors have continued their high standards of workmanship in this edition, and it is highly recommended as a reference for roentgen diagnosis. The English translation, which is forthcoming, should be of great interest to those who do not read German.

Lehrbuch der röntgenologischen Differentialdiagnostik. By Werner Teschendorf, M.D., Ed. 2, 1,946 illustrations. Stuttgart, 1950, Georg Thieme. Agents in U. S.: Grune and Stratton, New York.

This two-volume textbook of roentgen differential diagnosis is somewhat analogous to similiar texts of symptom differential diagnosis used in the field of internal medicine. As a rule, the author mentions a roentgen sign, such as clouding of a segment or lobe of one lung field, a defect in the mid-portion of the stomach, or a stenotic process in the colon; a number of possible conditions are given which may cause this roentgen sign and further roentgen studies are suggested which will aid in differentiating these conditions. In cases where the diagnosis is also dependent on correlation with other clinical findings, this is clearly brought out.

The text is primarily concerned with the differential diagnosis of internal diseases and, therefore, does not include the osseous system nor the head and neck. However, very thorough discussions of the lungs, cardiovascular system, diaphragm, gastrointestinal tract and genitourinary tract are included. Excellent reproductions of roentgenograms, indispensable to a text of this sort, are distributed throughout the two volumes.

For those who read German, and are using the roentgen method in diagnosis of internal diseases, this work is definitely recommended. It would seem quite worth while to have an English translation which would further extend its usefulness in this country.

The Normal Encephalogram. By Leo M. Davidoff, M.D., and Cornelius G. Dyke, M.D., Ed. 3. Pp. 240, with 156 illustrations. Philadelphia, 1951, Lea and Febiger. $6.00.

When the work entitled *The Abnormal Pneumoencephalogram* by Davidoff and Epstein was published, the second edition of Davidoff and Dyke's *The Normal Encephalogram* had just been exhausted. Dr. Davidoff then revised the latter text to make it a companion volume to the former.

The general structure of the book has remained unchanged. A few new illustrations have been added and the bibliography brought up to date.

As in the previous editions, there is a discussion of indications and contraindications for encephalography. Technique of encephalography including preparation of the patient, type and quantity of gas, roentgen technique, reactions to encephalography, and other general features of encephalography are discussed. Further chapters in the book deal with the cerebral ventricular system, the cerebral convolutions and sulci, the subarachnoid cisterns and their contents, and intracranial structures and their related fluid spaces. The discussion in each chapter is guided by what may be seen in the pneumoencephalogram and, as was stated in the preface to the first edition, might well be termed encephalographic anatomy.

There are 156 figures which consist of anatomic drawings and reproduction of roentgenograms. For the most part the roentgenograms reproduced are excellent.

This book is a valuable addition to the library of the roentgenologist, neurologist, neurosurgeon, pediatrician, or any other physician who is interested in the diagnosis of intracranial disease.

Contents—(Continued from front cover)

Intussusception in Adults. Charles H. Brown, M.D., and Arthur G. Michels, M.D., Cleveland, Ohio ---- 538

The Conservative Treatment of the Acute Form of Sigmoid Volvulus. Norman H. Isaacson, M.D., and Dan B. Greer, M.D., Washington, D. C. ---- 544

Carcinoma of the Thyroid and Nontoxic Nodular Goiter. Elmo J. Cerise, M.D., Spears Randall, M.D., and Alton Ochsner, M.D., New Orleans, La. ---- 552

A Suggested Terminology for Ligaments of the Groin; Their Clinical and Surgical Application in Repair of Hernias. Claud C. Burton, M.D., Dayton, Ohio ---- 562

Squamous-Cell Carcinoma of the Floor of the Mouth. Walter L. Mattick, M.D., Donald J. Meehan, M.D., and John P. Haberlin, M.D., Buffalo, N. Y. ---- 575

Case Reports

Hepatic Portal Arteriovenous Fistula. J. H. Strickler, M.D., Nathaniel Lufkin, M.D., and Carl O. Rice, M.D., Minneapolis, Minn. ---- 583

Homogenous Skin Grafts With and Without Adrenocorticotropic Hormones. Hans May, M.D., Richard S. Oakey, Jr., M.D., and George P. Pilling, IV, M.D., Philadelphia, Pa. ---- 590

Undesirable Sequela of Nonabsorbable Suture as Cystic Duct Ligature. J. Harvey Johnston, Jr., M.D., Jackson, Miss. ---- 597

Recurrent Gallstone Ileus. Eugene A. Noskin, B.S., M.D., and William J. Tannenbaum, M.D., Chicago, Ill. ---- 599

The Fate of the Incised Commissure in Mitral Stenosis. William H. Muller, Jr., M.D., Los Angeles, Calif. ---- 602

Jejunal Intussusception in Childhood Due to Tumor. Clarence J. Schein, M.D., and Leon Bluestone, M.D., New York, N. Y. ---- 609

Editorial

The Antibiotics and Liver Injury ---- 612

Recent Advances in Surgery

Pancreatitis: A Review. A. C. Ivy, Ph.D., M.D., Chicago, Ill., and G. E. Gibbs, Ph.D., M.D., Baltimore, Md. ---- 614

Book Reviews

Book Reviews ---- 643

NEW . . . ready-to-use antibiotic combination

Combiotic*

aqueous suspension

(Penicillin and Dihydrostreptomycin)

provides in each disposable cartridge or 2 cc. dose from vial

Penicillin G Procaine . . . . . .400,000 units

Dihydrostreptomycin (as the sulfate) . . . .0.5 Gm.

Supplied:

Single injection B-D† disposable cartridge syringes; 10 cc. "drain-clear" vials containing 5 doses.

clinically preferred . . .

in the treatment of certain mixed infections of the urinary tract, acute gonococcal infections, in selected cases of subacute bacterial endocarditis, and in surgical prophylaxis

because of these advantages . . .

- no mixing or reconstitution necessary
- microparticle suspension flows easily through 22-gauge needle
- drain-clear cartridge and vial means ability to withdraw full labeled volume
- buffered for stability; maintains full potency for one year under refrigeration

also available as Combiotic P-S (dry) in 3 cc. vials containing 300,000 units Penicillin G Procaine Crystalline, 100,000 units Buffered Penicillin G Sodium Crystalline, 1 gm. Dihydrostreptomycin as the sulfate; easily prepared by addition of sterile aqueous diluent.*

*Trademark, Chas. Pfizer & Co., Inc.
†Trademark, Becton, Dickinson and Company

Antibiotic Division **Pfizer** CHAS. PFIZER & Co., INC., *Brooklyn 6, N. Y.*